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# ABSTRACTS OF WORLD MEDICINE

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# ABSTRACTS OF WORLD MEDICINE



It is the aim of this journal to provide the reader with abstracts of all important articles appearing in medical periodicals published in every part of the world, and in this way to enable him to keep in touch with new developments throughout the whole field of medicine and in each of its special branches, including those aspects of surgery which are of particular concern to the physician.

More than 1,600 periodicals are surveyed, from which are selected for abstracting those papers which appear to make some useful contribution to the sum of medical knowledge or experience. Each paper is abstracted in sufficient detail to indicate to the general reader the nature and value of that contribution and to enable the specialist to assess its importance in relation to his own work and to decide whether the original article should be read in full. The author's own summary or an editorial summary published with the original article may occasionally be reproduced if it is suitable for these purposes, and the title and reference alone may be published in order to draw attention to a review article or other type of paper which cannot readily be abstracted.

The abstracts in each issue are grouped in sections according to subject and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together. The titles of papers written in languages other than English are given both in translation and in the original form. The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals*, as modified by *ISO Recommendation R4: International Code for the Abbreviation of Titles of Periodicals* (International Standards Organization, 1957), and in *World Medical Periodicals* (Second Edition, World Medical Association, 1957). The transliteration of authors' names from the Cyrillic alphabets is in accordance with *ISO Recommendation R9: International System for the Transliteration of Cyrillic Characters* (International Standards Organization, 1955).

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ABSTRACTS OF WORLD MEDICINE

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# Pathology

1364. **The Interaction of Plasma Proteins and Mucoid Substances in the Pathogenesis of Pulmonary Hyaline Membranes**

F. A. CARONE and W. G. SPECTOR. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **80**, 63–71, 1960. 6 figs., 27 refs.

The various theories of the mechanism of hyaline membrane formation are stated and experiments carried out at University College Hospital Medical School, London, on rats to see whether the interaction of various acidic polysaccharides and plasma protein in the pulmonary air spaces would give rise to structures looking and staining like hyaline membranes are described. In a first series of experiments pulmonary oedema was induced by the intraperitoneal injection of α-naphthyl thiourea (ANTU) and dextran sulphate, mucus, or meconium introduced into the trachea up to one hour later, resulting in most cases in the subsequent development of structures resembling typical hyaline membranes. The endotracheal introduction of amniotic fluid had the same result only if the fluid had previously been concentrated. In the absence of pulmonary oedema these substances had no such effect. In a further group of animals the endotracheal injection of dextran sulphate, nasal, tracheal, or bronchial mucus, or meconium together with rat plasma gave rise to similar membranes.

It is suggested that in the human foetus or newborn infant mucus from the bronchi or stomach, meconium, or amniotic fluid inhaled into the lung may form hyaline membranes by interaction with protein if pulmonary oedema is present. This theory is very fully discussed in the light of a comparison of the experimental and natural hyaline membranes. It is concluded that fibrinogen is the important constituent of oedema fluid which reacts with acidic mucopolysaccharides to form these membranes. *G. J. Cunningham*

1365. **Fatty-acid Distribution in Lipids of the Aortic Wall**

C. J. F. BÖTTCHER, F. P. WOODFORD, C. C. TER HAAR ROMENY-WACHTER, E. BOELSMA-VAN HOUTE, and C. M. VAN GENT. *Lancet* [*Lancet*] **1**, 1378–1383, June 25, 1960. 17 refs.

From the University of Leiden the authors present a further report of analysis of the lipids of the aortic wall at various stages of atherosclerosis, this analysis being more detailed than that in their preliminary study (*Lancet*, 1958, **2**, 1207; *Abstr. Wld Med.*, 1959, **25**, 306), since the use of polyester stationary phases has enabled them to separate fatty acids having the same chain length but different degrees of unsaturation. In all, 23 analyses were made of the intima and media of whole aortas obtained from subjects coming to necropsy. The degree of atherosclerosis was classified in four grades, for which the criteria are given, and the lipids were separated into phospholipids, free fatty acids, cholesterol esters, and glycerides, the fatty acids obtained from these 4 fractions being analysed by gas chromatography; the methods are described. The fatty acid patterns for each fraction, which are tabulated, were examined in relation to current theories of atherogenesis.

The chief findings were the marked increase in the control of polyunsaturated acids and decrease in that of all saturated acids with advancing atherosclerosis. These changes were most marked in the cholesterol ester fatty acid fraction, in which the proportion of polyunsaturated acids rose from 29 to 46% and that of saturated acids fell from 31 to 17%, the mono-unsaturated acids showing no significant change. These results do not support the hypothesis of Sinclair and other workers that cholesterol esters of saturated and/or mono-unsaturated acids tend to be deposited in the arterial wall in atheroma. The suggestion by Sinclair (*Lancet*, 1959, **2**, 789) that cholesterol esters of "abnormal" polyunsaturated acids, rather than true essential fatty acids, are to be found in atheroma is also refuted by the present authors' finding that the major polyunsaturated acid of the cholesterol esters was in fact at least 90% true linoleic acid and not an isomer of it. The fatty acids of the glyceride fraction and free fatty acid fraction showed similar but smaller changes to those of the cholesterol ester fraction. The changes in the phospholipids were irregular and did not follow the pattern of the other fractions; it is thought that they reflect the changes in the ratio of the different phosphatides to one another. Further analyses of the phospholipids are to be published later.

A comparison is made between the fatty acid components of the lipids deposited in the arterial wall and those found in plasma, as reported by various workers. The similarity of the fatty acid components of the cholesterol esters, free fatty acids, and glycerides in both plasma and deposits suggests that the deposits are derived from the blood. However, a marked difference was found in the fatty acids from the phospholipid of plasma and those from phospholipid of the deposits; this, it is suggested, may be due to synthesis of phospholipids in the deposits or to preferential accumulation of one of the phosphatides of the blood in atheroma. The authors are investi-

gating these possibilities by more detailed analysis, and are also studying the lipids of the coronary and cerebral arteries. *I. Berkinshaw-Smith*

1366. **Serum Detection of Carcinoma: Experience with the Schultz–Dale Technique**
E. HACKETT and E. GARDONYI. *British Medical Journal* [*Brit. med. J.*] **1**, 1785–1787, June 11, 1960. 9 refs.

From the Institute of Medical and Veterinary Science, Adelaide, S. Australia, the authors describe an attempt to apply the Schultz–Dale technique for the diagnosis of cancer to sera from 49 proved cases of carcinoma. They found that in 23 (47%) the result was positive, in 8 it was inconclusive, and in 18 was negative. They therefore conclude that the claims of Makari (*Brit. med. J.*, 1955, **2**, 1291, and 1958, **2**, 358; *Abstr. Wld Med.*, 1956, **19**, 417, and 1959, **25**, 146) that the test has an accuracy of about 90% have not been substantiated. However, the present results are considered to offer further confirmation of the two main features of Makari's work: (1) that there is a difference between the responses of some guinea-pigs immunized with carcinoma antigens from non-carcinomatous organs, and (2) that these responses are excited by sera from some patients with carcinoma and not by sera from healthy subjects. *L. A. Elson*

## HAEMATOLOGY

1367. **The E.S.R. in a New Dress**
J. B. DAWSON. *British Medical Journal* [*Brit. med. J.*] **1**, 1697–1704, June 4, 1960. 12 figs., 19 refs.

The investigation here reported from the University of Edinburgh was carried out in an attempt to establish the most convenient method of determining the erythrocyte sedimentation rate (E.S.R.), some of the various modifications of the classic Westergren method being suspected of serious anomalies. After a brief historical review the author discusses the theoretical and practical factors concerned in determining the final numerical value of the E.S.R. and gives a precise definition of the aims of his study. The materials and methods employed are then described in detail. Standard Westergren pipettes were employed and these were usually suspended from hooks according to the method of Duxbury, the distal end being blocked by a rubber cap. It was shown that lateral swinging of the suspended pipette did not affect the result.

The results of the various experiments are analysed statistically and expressed graphically. It is concluded that the best method of determining the E.S.R. is to dilute 2 ml. of a sequestrenized blood sample with one-quarter its volume of isotonic (3·8%) sodium citrate solution and then examine the rate of fall of the erythrocytes in a freely suspended tube. Good correlation was obtained between this method and a standard method in which oxalated blood diluted with 3·8% sodium citrate was used, and a similarly good correlation was obtained with the classic Westergren method. The use of undiluted blood to which a solid anticoagulant has been added was shown to give unreliable results with the Westergren pipette. One advantage of "sequestrene" (EDTA) is that deterioration, especially of the nuclei and membranes of abnormal blood cells, is less than with other anticoagulants so that other haematological investigations may be carried out on the same blood sample. It was noted that the use of relatively dirty pipettes which had simply been washed in tap water and allowed to dry did not affect the accuracy of the results. On the other hand increased accuracy was obtained when microburettes and accurate pipettes were employed for making the 1:4 dilution of blood and anticoagulant.

From a review of the literature, supported by his own experimental results, the author deduces that Westergren's original normal ranges for the E.S.R. (male adults 0 to 5 mm., female adults 0 to 10 mm. in one hour) are too narrow and that 5 mm. should be added to the upper limit in each case. However, in adults over 50 higher values may be normal, while in pregnancy the normal range is up to 45 mm. in one hour. Normal newborn infants have a low E.S.R.—about 2 mm. in one hour by the standard method. *A. Brown*

1368. **Immunologically Different "Normal" Fetal Hemoglobins**
W. F. MCCORMICK and R. H. WALKER. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **33**, 500–504, June, 1960. 4 figs., 20 refs.

In this paper from the University of Tennessee, Memphis, experimental immunological evidence is brought forward which is held to indicate the existence of different types of normal foetal haemoglobin. Guinea-pigs were injected with a single foetal haemoglobin and the antiserum produced was tested by the agar diffusion precipitation technique. It was found to react with some samples of human foetal haemoglobin, but not with others. When pooled foetal haemoglobin was injected a polyvalent antibody was obtained which precipitated all samples of foetal haemoglobin. These foetal haemoglobins could not be distinguished by means of the alkali denaturation test, paper electrophoresis, or other techniques at present available. The authors state that the antibody produced in the guinea-pig resulted solely from foetal haemoglobin and not from erythrocyte stroma, since the latter cannot pass through the Seitz filter used in preparing the haemoglobin solution.

[The authors do not seem to take into account the fact that a water-soluble extract of erythrocytes contains, in addition to haemoglobin, certain other proteins whose presence may well have been involved in the reactions observed.] *H. Lehmann*

1369. **The Cellular Distribution of Foetal and Adult Haemoglobins**
C. S. BREATHNACH. *Irish Journal of Medical Science* [*Irish J. med. Sci.*] 286–290, June, 1960. 3 figs., 12 refs.

Whereas dried blood films from adults normally show a complete elution of haemoglobin from the erythrocytes when washed for a few minutes in acid phosphate buffer, this is not so when the cells contain foetal haemoglobin. If adult and foetal cells are mixed and eluted with acid buffer subsequent staining with eosin will show erythro-

cyte " ghosts " in the case of the adult cells and clearly stained corpuscles in the case of the foetal cells. This phenomenon is not due to some property of the membrane or stroma of the erythrocytes, since the differential elution can be equally well produced when filter paper is soaked with the haemoglobin solutions and subsequently treated with acid buffer.

In the present investigation, reported from University College, Dublin, the percentage of cells shown to contain foetal haemoglobin by staining and the total percentage of foetal haemoglobin in samples of cord or capillary blood from infants up to 17 weeks old were remarkably alike. The author concludes that there are two erythrocyte populations in early infancy, one containing only foetal haemoglobin and one containing only adult haemoglobin.

[It has to be pointed out that certainly in some cases of thalassaemia the presence of foetal haemoglobin and adult haemoglobin can be demonstrated in all the erythrocytes, and it is of course well known that in the sickle-cell trait virtually all the erythrocytes contain a mixture of adult and sickle-cell haemoglobin.]

*H. Lehmann*

1370. **Clinical Significance of the Sedimentation Rate of Leukocytes.** [In English]

E. Storti, E. Lusvarghi, L. Bellesia, and P. Mucci. *Acta medica Scandinavica* [*Acta med. scand.*] **167**, 1–21, 1960. 10 figs., 11 refs.

At the University of Modena, Italy, the leucocyte sedimentation rate (L.S.R.) was estimated in 300 healthy adults aged 18 to 60 years and 133 patients with various disorders, including leukaemia and various types of tumour. The technique involves setting up a column of diluted leucocyte-rich plasma on top of a column of undiluted leucocyte-free plasma, both contained in a vertical cylindrical tube 20 cm. in length and 0·7 cm. in diameter. Samples of the plasma are withdrawn after one and 2 hours by means of a needle and syringe through rubber-plugged holes set in the side of the tube at 15-mm. intervals; the level of the sedimentation front is determined by microscopical examination. The L.S.R. was slightly increased in 40 untreated cases of chronic leukaemia and greatly increased in 10 of acute leukaemia, but was not increased in cases of carcinoma until hepatic metastases developed. In lymphosarcoma and reticulosarcoma the rate was also normal, whereas in Hodgkin's disease in relapse or at the time of the first manifestation leucocyte sedimentation was accelerated. In patients with tuberculous infection or acute or chronic bacterial sepsis the leucocyte sedimentation usually paralleled the erythrocyte sedimentation rate.

In contrast to erythrocyte sedimentation, it has been shown that cellular rather than plasma factors are responsible for acceleration of leucocyte sedimentation, except that a gross increase in plasma fibrinogen content does increase it. The authors suggest that this new test will be of value in differentiating pulmonary and mediastinal lesions (tuberculosis, Hodgkin's disease, and carcinoma), in helping to determine if the liver has yet been invaded by carcinoma, in differentiating lympho- or reticulosarcoma from Hodgkin's disease, and in measuring the effectiveness of treatment in Hodgkin's disease.

[This test is of theoretical interest, but it would appear to be difficult to find a useful place for such a non-specific investigation in the face of the many other available techniques.] *T. B. Begg*

1371. **Measurement of Overall Coagulability during Coumarin Treatment with Reference to the Quick Test.** [In English]

M. Verstraete, C. Vermylen, and J. Vandenbroucke. *Acta medica Scandinavica* [*Acta med. scand.*] **167**, 127–138, 1960. 7 figs., 31 refs.

The authors note that the Quick test for one-stage prothrombin time does not measure changes in the Christmas factor (Factor IX), since this makes no contribution to one-stage prothrombin time, and it may also miss other factors. At the University of Louvain, Belgium, they have investigated a variety of other tests and here describe the sodium chloride tolerance test of Jürgens (*Blut*, 1956, **2**, 301) which seemed most worth consideration. This test depends on the fact that the clotting process can be retarded by increasing the concentration of ions in the clotting mixture; this is achieved by recalcifying the plasma under test with a mixture of 2·5% sodium chloride in 0·05 M calcium chloride, the result being expressed as the percentage increase in clotting time compared with the normal time. Changes in the test reflect changes in the Stuart–Prower and Christmas factors, and therefore the test is a valuable complement to the usual techniques, especially for the control of patients receiving long-term anticoagulant therapy.

[The authors apparently did not investigate Owren's latest modification, the " thrombotest ", which does take account of the Christmas factor.] *M. C. G. Israëls*

## MORBID ANATOMY AND CYTOLOGY

1372. **The Histopathology of Cerebral Rheumatism.** (К гистопотологии мозгового ревматизма)

K. N. Čalisova. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **60**, 269–272, No. 3, 1960. 4 figs., 8 refs.

This communication reports a series of 16 cases of cardiovascular rheumatism in which lesions of the brain developed, usually as a sequel to diffuse thrombovasculitis. One case is described in detail.

A woman of 33 who had suffered from rheumatism from childhood and had had recurrent attacks of carditis, developed a sudden paralysis of the right arm and leg, with nuclear paralysis of the left facial nerve. This cleared up in 4 days, but 2 months later she developed right hemiplegia and aphasia, with pseudobulbar symptoms. This again remitted, but after 7 months the bulbar symptoms recurred, with severe headache, vomiting, and at times loss of consciousness. On admission to hospital she was febrile and the erythrocyte sedimentation rate was 38 mm. in one hour. There were signs of mitral disease and congestive cardiac failure; the blood

pressure was 105/70 mm. Hg. Left laryngeal paralysis was present and she had a right hemiplegia. She did not respond to treatment and died a month after admission.

At necropsy the diagnosis of mitral valvular disease was confirmed and in addition the myocardium showed numerous foci of fibrosis. There were multiple haemorrhagic infarcts of the lungs and kidneys. The cerebral hemispheres showed large areas of softening with cyst formation. The vessels of the cerebral cortex, cerebellum, subcortical ganglia, pons, and medulla showed advanced vasculitis with thickening and often calcification of the walls, narrowing of the lumen, and hyalinization of the muscular coat; the collagen fibres were swollen and stained poorly. In some areas there was oedema of the perivascular spaces. Diffuse proliferation of the glia was observed. Thus in this case the brain symptoms resulted, not from embolism, but from a diffuse vascular disease of rheumatic nature.

*L. Firman-Edwards*

1373. **The "Benign" Form of Hodgkin's Disease (Hodgkin's Paragranuloma)**

C. J. E. WRIGHT. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **80**, 157–171, 1960. 18 figs., 24 refs.

A review, carried out in the Department of Pathology, University of Leeds, of surgical material from 339 cases of Hodgkin's disease showed that Hodgkin's paragranuloma was present in 26 (1 in 13). In 24 of these for which records were complete, a study of the clinical course in relation to the biopsy and post-mortem findings revealed a group of cases with a certain histologically variable but fairly well-defined pattern and a good prognosis, 7 of the patients being alive 10 to 35 years after the condition was first diagnosed. The author points out that although, characteristically, only a few lymph nodes may be affected at first, the disease may eventually become generalized. There was generalized spread in 6 of the 24 patients, 4 of whom are dead.

The importance, from the point of view of prognosis, of differentiating this group of cases from those of Hodgkin's disease and lymphosarcoma is emphasized.

*J. B. Wilson*

1374. **Lymph Nodes in Human Bone Marrow.** (Die Lymphknötchen im menschlichen Knochenmark)

W. WERNER. *Frankfurter Zeitschrift für Pathologie* [*Frankfurt. Z. Path.*] **70**, 398–408, 1960. 5 figs., 36 refs.

Working at the Pathological Institute of the University of Griefswald the author has determined the frequency of the occurrence of lymph nodes in the marrow of the vertebrae and ribs. Both smears and sections of necropsy specimens from 345 unselected subjects aged 0 to 87 years were examined. Lymph nodes were seen in 21% of these cases compared with a frequency of 3 to 62% recorded by other authors.

The lymph nodes were always in the cellular part of the marrow and never in fatty tissue. Their average diameter was 250 $\mu$. They consisted mainly of small lymphocytes with a reticular framework. Germinal centres were occasionally seen. Nodes were found in the vertebrae, sternum, ribs, and long bones in decreasing order of frequency. The youngest subject in whose marrow lymph nodes were found was 10 months old, and the frequency of their occurrence was found to increase with age. On combining the author's series with those reported by others it was found that lymph nodes were present in the marrow of 113 out of 682 individuals under 40 and of 282 out of 784 over 40. The only pathological correlation that could be discovered was a higher incidence in cases of accidental death than in patients dying from natural causes.

*G. Loewi*

1375. **A Study of Certain Microscopic Features in Regional Enteritis, and Their Possible Prognostic Significance**

J. I. ANTONIUS, F. E. GUMP, R. LATTES, and M. LEPORE. *Gastroenterology* [*Gastroenterology*] **38**, 889–905, June, 1960. 13 figs., 14 refs.

In a histological study of 56 cases of regional enteritis [at the Columbia–Presbyterian Medical Center, New York] it was found that "aberrant pyloric glands" occurred in 58·9% of the specimens examined, "epithelioid and giant cell granulomas" in 37·5%, "neuromatous" lesions in 14·3%, and vascular arterial lesions in 16·1%. No satisfactory clinical–pathological correlation could be established between these histological lesions and prognosis, in terms of postoperative recurrences after a minimal 5-year follow-up period.

The pathogenesis and the specificity of these four histologic lesions are not clear. The "aberrant pyloric glands" are quite likely an acquired rather than a congenital lesion. They may represent an adaptation of the intestinal mucosa to an abnormal environment. In this series the granulomatous lesions were never associated with systemic sarcoidosis or with demonstrable acid-fast bacteria or fungi. The "neuromatous" lesions are probably an acquired, diffuse hyperplasia of the myenteric neural system, almost certainly different from the common amputation neuroma. The occasional vascular arterial lesions observed in this series of cases seemed to be nonspecific responses to inflammation, secondary to the chronic ulcerative disease.

It appears that none of these histologic lesions is pathognomonic for the entity known as regional enteritis. —[Authors' summary.]

1376. **The Mechanism of Malarial Hepatomegaly and Its Relationship to Hepatic Fibrosis**

J. H. WALTERS and I. A. MCGREGOR. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **54**, 135–145, March [received June], 1960. 6 figs., 18 refs.

The authors examined liver biopsy specimens obtained by the Roholm–Iversen technique from 20 Gambian children aged 3 to 3½ years, 9 of whom (Group A) had received antimalarial drugs from birth, whereas the remaining 11 (Group B) had been given drugs only to control attacks of malaria. Only in one child in Group A was the liver enlarged, while in Group B both liver and spleen were enlarged in all cases. The groups were otherwise alike so far as nutritional status and parasitological findings at the time of the investigation were concerned. The biopsy specimens were fixed immedi-

ately in 80% ethyl alcohol and later stained with haematoxylin and eosin and by Gomori's silver impregnation method.

Some fatty infiltration of hepatic cells [unspecified] was observed in one child of Group A and in 3 of Group B. No other cellular changes were observed; there was no hyperplasia. Evidence of an inflammatory reaction in the form of " an infiltration or aggregation of mononuclear cells, polymorphonuclear leucocytes and histiocytes in the portal tracts and sinusoids " was found in 5 cases in Group A and in all in Group B. (The authors suggest that malarial pigment may have constituted an irritant factor.) As expected, there was an increase in both the size and number of Kupffer cells in all specimens from Group B, the cells being loaded with black pigment. In all specimens from Group B there was an increase in the calibre of the sinusoids. Numerical evaluation of this feature was carried out by projecting the image of an area of each section, under standard magnification, on to a standard-sized circular filter paper and tracing the outline of the sinusoids. The paper was then weighed, the sinusoidal area cut out, and the residuum weighed again, figures representing the ratio hepatic area:sinusoidal area and sinusoidal area as a percentage of the whole being obtained in this way. The mean relative area of sinusoidal space, calculated by both methods, was greater in Group B than in Group A, the difference being highly significant.

On examination of the silver-impregnated specimens an excess of fibrous tissue in the portal tracts was judged to be present in 6 specimens from children in Group A (including one with congenital syphilis) and in 9 from children in Group B. " Abnormal outgrowths " of fibres from the margins of the portal tracts were present in all cases in Group B, but in only the syphilitic case in Group A. Some thickening of the longitudinal fibres in the sinusoidal wall was seen in one specimen in Group B; in this specimen and in one other in the same group there was also some excess of fine encircling fibres. Slight thickening of the central vein was noted in 3 specimens in Group A (out of 7) and in 3 in Group B (out of 11).

The authors conclude, in agreement with other workers, that the pathological processes of chronic malarial hepatomegaly include hyperplasia of the perilobular connective tissue and " capillary dilatation ". The latter is the most important factor. They did not find evidence of hyperplasia in their material. They consider that in the absence of liver cell damage from other causes the periportal fibrosis does not extend farther into the lobule.

*B. G. Maegraith*

1377. **Changes in Hepatic Structure in Wilson's Disease**
P. J. ANDERSON and H. POPPER. *American Journal of Pathology* [*Amer. J. Path.*] **36**, 483–497, May, 1960. 11 figs., 19 refs.

In a study undertaken at the Mount Sinai Hospital, New York, in order to gain further knowledge of the pathogenesis, the histological appearances in the liver in 20 cases of hepatolenticular degeneration (Wilson's disease) are described. Cirrhosis was present in 19 and was post-necrotic in type, as opposed to the fine granular type seen in Laënnec's cirrhosis. Most of the specimens were obtained post mortem, but a few by biopsy.

In all the necropsy material the fibrosis was irregular, with stromal collapse and formation of septa of varying width. The lobular pattern was preserved in many of the nodules, and there was conspicuous parenchymal regeneration. In one biopsy and 4 necropsy specimens the disease was in the arrested stage, and the parenchyma showed little abnormality excepting for focal necrosis. The border between the nodules and septa was sharp and the portal tracts showed only slight inflammatory reaction. In 6 necropsy specimens a partially arrested stage was seen; here the nuclei of many parenchymal cells located peripherally in the nodules were markedly distended, being enlarged up to 20 $\mu$ and containing glycogen. Also, especially in the smaller nodules, there were large regenerating liver cells with giant nuclei. There was some mononuclear leucocyte infiltration and areas of disintegrating liver cells with conspicuous fatty metamorphosis were noted. The active stage of the disease was observed in 7 necropsy specimens; in 6 of these large nuclei containing glycogen were found, and in 5 they were abundant. Fatty metamorphosis was present in all but one case, with disintegration of fatty cells, while the cytoplasma frequently showed acidophilic coagulation; neighbouring Kupffer cells were large and contained cellular debris. Regeneration was prominent. In one further necropsy specimen there was acute parenchymal breakdown, and in one biopsy specimen precirrhotic fatty metamorphosis was seen. Two biopsy specimens taken from an apparently healthy sibling of a patient with Wilson's disease showed normal appearances, except that nuclei distended with glycogen were seen in the periphery of the lobules.

In a control group of 15 cases of active post-necrotic cirrhosis distension of nuclei was observed in 3, fatty metamorphosis in 8, and in one case only was there necrosis and breakdown of fatty cells, this occurring in the absence of enlarged Kupffer cells.

*W. H. Horner Andrews*

1378. **Myocardial Infarction in Women: a Study of Autopsy Populations**
F. GOODALE, W. A. THOMAS, and R. M. O'NEAL. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] **69**, 599–604, June, 1960. 1 fig., 14 refs.

It has up till now been generally held that acute myocardial infarction is much commoner in men than in women, the ratios quoted varying between 6:1 and 3:1. In recent years, however, post-mortem studies have suggested that this difference no longer exists. The present paper, from Washington University School of Medicine, St. Louis, reports a review of the incidence of acute myocardial infarction as ascertained at three large medical centres, widely separated geographically, and based on a total of 13,485 records of necropsies performed on adults aged over 20 years of age, 4,436 being from Barnes Hospital, St. Louis, for the period 1940–54, 5,460 from Massachusetts General Hospital, Boston, for the period 1945–54, and 3,589 from the Radcliffe Infirmary, Oxford, for the period 1946–53. The criteria for diagnosing

acute myocardial infarcts were muscle necrosis and an inflammatory cellular reaction, thus excluding very old or very recent infarcts. The clinical records from Barnes Hospital, St. Louis, were also reviewed and data tabulated for age and sex in four groups as follows: (1) all deaths; (2) all deaths with clinically diagnosed acute myocardial infarcts; (3) all patients with acute myocardial infarction discharged alive; (4) a random sample consisting of 3 out of every 200 patients discharged alive during 1942–54.

It was shown that the only difference in sex incidence of acute myocardial infarction found at necropsy occurred in subjects below the age of 50 years. Even in those under this age the ratio of men to women was only 2·87:1 (the ratio for all ages being 1·17:1). There was very little difference between the results obtained at the three hospitals. The sex incidence of acute myocardial infarction in fatal cases diagnosed clinically agreed closely with the figures obtained from the necropsy records, the ratio of men to women being 2·2:1 among patients aged 50 and over and 1·2:1 in the whole group. One striking difference between the sexes in regard to acute myocardial infarction, however, was in the number of patients discharged from hospital alive: thus in this category there were 3½ times as many men as women and the ratio of men to women under 50 years of age was 12:1.

The authors discuss this difference and point out that it may be due to failure to diagnose mild acute myocardial infarction in women, perhaps because it is not thought of in their sex. They conclude that the post-mortem incidence of acute myocardial infarction is now similar in men and in women, except for the small percentage of infarcts occurring in patients under 50 years of age; but they stress that " great caution is necessary in using data derived from autopsies for drawing conclusions regarding the general population because immeasurable factors of selection are present ".

*I. Berkinshaw-Smith*

1379. **Nuclear Changes in Squamous Cells from Buccal Mucosa in Pernicious Anaemia**

P. C. FARRANT. *British Medical Journal* [*Brit. med. J.*] **1**, 1694–1697, June 4, 1960. 6 figs., 19 refs.

The author, working at Bristol Royal Infirmary, studied the nuclear abnormalities in the oral squamous mucosa in 25 cases of pernicious anaemia before and after treatment. Films of scrapings of oral mucosa were stained by the May–Grünwald–Giemsa technique and projected, a microscope and a powerful light source being used so as to give a magnification of ×1,000. The means of the measurements of the long and short axes of the oval-shaped nuclei were used for comparison.

It has previously been shown (Farrant, *Lancet*, 1958, **1**, 830; *Abstr. Wld Med.*, 1958, **24**, 355) that in untreated pernicious anaemia the nuclei are irregular in shape and usually abnormally large, but that the degree of enlargement is independent of the degree of anaemia. In the present series after treatment with vitamin $B_{12}$ (cyanocobalamin) there was a slight increase in both axes in 4 cases and a diminution in size of the short axis only in 2; in the remaining 19 cases there was a significant decrease in nuclear size, the decrease being greater in the short axis than in the long, and in irregularity of shape. In many cases the nuclear chromatin became more pyknotic and dense. The change to normal size and shape of the nuclei took only a few days once treatment was started.

The possible significance of these findings is discussed, the author considering that there is much evidence of a disorder of nucleic acid metabolism in this type of anaemia.

*H. Caplan*

1380. **Study of Renal Ischaemic Tubular Atrophy in 79 Patients with Arterial Hypertension**

R. LEFEBVRE and J. GENEST. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **82**, 1249–1253, June 18, 1960. 2 figs., 11 refs.

This study was undertaken in order to evaluate the degree of ischaemic tubular atrophy (I.T.A.) in an unselected consecutive series of 79 hypertensive patients. I.T.A. is characterized histologically by crowded intact glomeruli surrounded by small, atrophic but viable tubules of very narrow lumen lined with cuboidal cells, usually with clear cytoplasm. Of these patients, who were all treated at the Hôtel-Dieu Hospital, Montreal, during the years 1953 to 1958, the kidneys in 71 cases were examined at necropsy and in the other 8 cases unilateral nephrectomy was carried out for relief of hypertension.

Varying degrees of I.T.A. were found in 45 patients (63%) in the necropsy series; in 3 of the 7 most severely affected cases the lesions were unilateral. It is noteworthy that only 20 out of 57 cases of essential hypertension showed significant areas of I.T.A., whereas in all 14 cases of renal hypertension these lesions were found. Histological evidence of pyelonephritis was found in 28 (62%) of the 45 cases with I.T.A., while of the 18 cases of malignant hypertension 14 were associated with pyelonephritis and 2 with chronic glomerulonephritis. Of the 8 kidneys removed at operation ischaemic tubular atrophy was found in 6. In all 79 cases there was close correlation between the degree of I.T.A. and the amount of renal vascular sclerosis, the severity of hypertension, the degree of retinopathy, and the extent of decrease in renal function and reduction in weight of kidneys. The authors state that a control study is now under way to determine the significance of these lesions of I.T.A. in relation to hypertension.

*A. W. H. Foxell*

1381. **The Frequency of Differentiation in Oat-cell Carcinoma of the Lung**

J. B. WALTER and D. M. PRYCE. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **80**, 121–125, 1960. 9 figs., 24 refs.

The histological classification of carcinoma of the lung is made confusing by the failure of some workers to recognize that oat-cell tumours may be differentiated by showing the presence of rosettes or tubules. In the present study, reported from the Royal College of Surgeons of England and St. Mary's Hospital, London, 127 surgically resected oat-cell carcinomata were examined. They were distinguished from undifferentiated adenocarcinomata by the individual cytological structure and

by the fact that they never stained positively for mucus. The characteristic features of tubular differentiation were found in 12 cases, rosette formation in 72, and basal-cell palisading in 82. The differential diagnosis of oat-cell tumours from neuroblastomata and other similar tumours is discussed.

[This paper is important in view of recent attempts to correlate histological types of lung cancer with aetiological factors.] *G. J. Cunningham*

1382. **Congenital Cystic Disease of the Lungs and Its Classification**

A. D. MOFFAT. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **79**, 361–372, 1960. 21 figs., 28 refs.

This paper from Stobhill General Hospital, Glasgow, presents a study of 9 cases of cystic lung, 8 of which were investigated by macroscopical and histological techniques, including in some cases serial section. The patients ranged in age from 2 hours to 2 years, and the author concludes that in all the condition was congenital in nature. Careful histological examination enabled the cases to be divided into three groups according to whether the cysts had been derived from (*a*) the air passages, (*b*) the lymphatics, or (*c*) pleural elements. The reasons for the classification of each of the cases are given in detail.

[This is an excellent study. The structure from which the cysts were derived could be identified with some certainty, but the actual aetiology of the condition is much more doubtful in such a purely histological study. In some of the cases the disease occurred so early in life that a congenital origin appears certain, but in others an acquired aetiology cannot be excluded with certainty.] *G. J. Cunningham*

1383. **Problems in the Pathologic Diagnosis of Carcinoma of the Thyroid**

R. C. HORN JR. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] **69**, 481–492, May, 1960. 12 figs., 14 refs.

The difficulties in the histopathological diagnosis of certain types of tumour of the thyroid gland are now well recognized. In this paper from the Henry Ford Hospital, Detroit, the author reviews 68 cases of thyroid disease treated surgically which presented such problems.

Carcinomata were differentiated from atypical adenomata on the basis of vascular or capsular invasion. In cases of " thyroiditis " the striking papillary hyperplasia, marked pleomorphism with bizarre nuclei, and an appearance simulating invasion all presented diagnostic problems. The author suggests that a papillary pattern can be safely considered benign in the presence of the other characteristic features of thyroiditis; the diffuseness of apparent invasion is usually strongly suggestive of fibrosis and of the trapping of epithelial elements rather than true invasions. The bizarre features seen in Hürthle cells actually occur more frequently in benign than in malignant lesions of the thyroid, excluding of course true anaplasia. Lymphoid infiltration may be so dense that lymphoma must be considered in the differential diagnosis. Hyperplasia of extreme degree is difficult to differentiate from carcinoma, especially if associated with atypical nodules or an atypical cytological pattern. It is emphasized that knowledge of a history of severe Graves's disease and of any treatment with iodine or other antithyroid agent is essential in these cases.

On the basis of these criteria 58 of the 68 cases were classified with reasonable assurance, presumptive diagnoses were made in a further 7, but 3 cases remained undiagnosable. The paper contains some 27 photomicrographs illustrating various types of thyroid disorder. *H. Caplan*

1384. **Microlithiasis (Calcospherites) and Carcinoma of the Thyroid Gland**

J. G. BATSAKIS, R. H. NISHIYAMA, and C. R. RICH. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] **69**, 493–498, May, 1960. 1 fig., 31 refs.

In this report, from the University of Michigan Medical School, Ann Arbor, evidence is presented to support the hypothesis that the presence of calcospherites (psammoma bodies) is of assistance in differentiating benign from malignant thyroid neoplasms. An average of 10 sections from each of 819 thyroid glands removed at operation were examined.

Calcospherites, seen as blue-staining, round, usually laminated bodies 25 to 75 $\mu$ in diameter, were found in 84 out of 207 cases of malignant epithelial neoplasm of the thyroid gland and in 10 of 612 non-malignant thyroid tumours. [The high ratio of carcinoma is more apparent than real, since the authors were primarily investigating cases of thyroid carcinoma.] Calcospherites were particularly prominent in papillary neoplasms, but they occurred in all types of primary carcinoma of thyroid. Sex and age of the patient or previous operative procedures had no bearing on the presence of calcospherites. The authors conclude that the identification of calcospherites may serve as a diagnostic but not as a prognostic aid in thyroid carcinoma and as such should be added to the various diagnostic criteria employed in the diagnosis of such lesions. *H. Caplan*

1385. **Influenzal Encephalopathy and Post-influenzal Encephalitis: Histological and Other Observations**

J. G. HOULT and T. H. FLEWETT. *British Medical Journal* [*Brit. med. J.*] **1**, 1847–1850, June 18, 1960. 6 figs., 8 refs.

The histological findings in the central nervous system of 4 children and one adult who died from encephalitis associated with influenza are described. The children were aged 5 to 13 years and the adult 44; the clinical details of these cases have been described elsewhere (Flewett and Hoult, *Lancet*, 1958, **2**, 11; *Abstr. Wld Med.*, 1959, **25**, 10). The changes observed in the children's brains were (1) scanty lymphocytic infiltration of the perivascular spaces of the brain and meninges, and (2) microglial nodules replacing isolated Purkinje cells and cells of the spinal grey matter. The findings in the adult were those of acute haemorrhagic leucoencephalitis. Only in this last case was the diagnosis of influenzal infection not confirmed virologically.

*J. B. Cavanagh*

# Microbiology and Parasitology

1386. **Screening for *Salmonella* with Bacteriophage**
M. J. PICKETT and S. M. LAUGHNER. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **33**, 298–302, April, 1960. 10 refs.

In 1954 Cherry *et al.* (*J. Lab. clin. Med.*, **44**, 51; *Abstr. Wld Med.*, 1955, **17**, 177) reported highly satisfactory results in the identification of organisms of the *Salmonella* group by means of the " O–1 " bacteriophage of Felix and Callow (*Brit. med. J.*, 1943, **2**, 127). The present authors, working at the University of California, Los Angeles, have used a pooled suspension of this O–1 phage and an adapted Group-D phage of Wassermann and Saphra (*J. Bact.*, 1955, **69**, 97). The media and methods employed are fully described. Rapid detection of *Salmonella* species was possible and because the procedure is labour-saving, reliable, and gives results within 4 to 6 hours the authors advocate its use as a screening test, particularly in epidemiological surveys. In tests carried out on 133 strains of *Salmonella* and also members of the Arizona group of enterobacteria in which representatives of all the important species were included, only 3 strains were found to be resistant. The authors point out that their procedures for increasing the sensitivity of this screening test did not affect its specificity.

*R. Hare*

1387. **Experimental Vaccination against Measles. I. Tests of Live Measles and Distemper Vaccine in Monkeys and Two Human Volunteers under Laboratory Conditions**
A. J. F. SCHWARZ, P. A. BOYER, L. W. ZIRBEL, and C. J. YORK. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **173**, 861–867, June 25, 1960. 2 figs., 13 refs.

In these experiments carried out on cynomolgus monkeys and 2 child " volunteers " (aged 2½ and 4 years respectively) the Edmonston strain of measles virus passaged in chick embryo tissue cultures 17 times was used as a living vaccine. Of the 4 monkeys inoculated orally, 12 intramuscularly, and 12 intercerebrally all developed neutralizing and complement-fixing (C.F.) antibodies to measles virus. None of the monkeys showed any signs of illness nor did susceptible monkeys kept in the same cages as the infected monkeys develop antibodies. Blood specimens and throat washings taken every second day for 15 days and inoculated into human amnion or human heart tissue cultures, as sensitive indicators of virus, resulted in the isolation of the virus from the blood and throat of a few monkeys in each group. The 2 children, neither of whom possessed antibody to measles, were inoculated intramuscularly with the vaccine. A week later both had a raised temperature, a lowered leucocyte count, and mild tonsillitis, but no rash or Koplik's spots were seen. Virus was not isolated from their throats, but was isolated from the blood of one child after a week. Both children developed neutralizing and C.F. antibodies. The authors conclude that monkeys are not as sensitive to this virus as children, and that experiments with living vaccines must therefore be performed on human volunteers.

Since the virus causing canine distemper is known to be immunologically related to the measles virus 6 monkeys which developed specific neutralizing antibody after an injection of live distemper virus (also grown in chick embryo tissue culture) were challenged with measles vaccine. Antibody titres against distemper rose quickly, as with a booster dose of antigen, but those against measles showed only a typical primary response. On the other hand, however, when 3 monkeys which had developed measles antibody after vaccination with measles virus were given distemper virus, neutralizing antibodies to distemper again increased rapidly, but no rise in measles C.F. antibody was observed. It appears, therefore, that the strain of distemper virus used lacked the antigenic component which causes the production of measles antibodies, whereas measles virus stimulates the production of antibodies against both measles and distemper.

*Janice Taverne*

1388. **Experimental Vaccination against Measles. II. Tests of Live Measles and Live Distemper Vaccine in Human Volunteers during a Measles Epidemic in Panama**
M. T. HOEKENGA, A. J. F. SCHWARZ, H. C. PALMA, and P. A. BOYER. *Journal of the American Medical Association* [*J. Amer. Med. Ass.*] **173**, 868–872, June 25, 1960. 2 figs.

This paper describes a field trial of the live measles and distemper vaccines described above [see Abstract 1387] which was carried out in 1959 during a measles epidemic among families living in the banana plantations of western Panama, in which 1,611 individuals, most of them children, who had no clinical history of measles were offered vaccination, the control group consisting of those who refused it. Of these subjects 453 were given one dose of live-virus measles vaccine intramuscularly, 388 were given the distemper vaccine, and 770 acted as controls. No reactions to distemper vaccination were observed, nor to the measles vaccine in those over 5 years of age. About 80% of the children under 5, however, suffered a fever about a week after measles vaccination, some developing a rash and a few Koplik's spots. In 4 cases the reactions were severe enough to require hospital treatment. The severity of reactions to the vaccine appeared to be related to the degree of undernourishment.

During the 4 months following vaccination 0·7% of those who received the measles vaccine developed measles, against 9% of the controls. Of 243 vaccinated children under 5 years of age 0·8% got measles, as compared with 15·5% of 103 unvaccinated children. Less protection was provided by the distemper vaccine, 3·6% of older

inoculated children catching measles, compared with 6% of the controls, while 4·1% of 221 children under 5 years of age developed measles, compared with 12·1% of 116 similar controls. Thus distemper vaccine was effective only in children under 5, and although the measles vaccine was undoubtedly effective, the authors conclude that the high incidence of reactions limits its usefulness. *Janice Taverne*

1389. **The Phenomenon of Inhibition of Circulating Antibodies by Hyperimmunization.** (Le phénomène de l'inhibition d'anticorps circulants par hyperimmunisation)
J. GRAS. *Revue d'immunologie et de thérapie antimicrobienne* [*Rev. Immunol. (Paris)*] **24**, 354–366, April–June, 1960. 6 figs., 8 refs.

The phenomenon of " immunological paralysis "—the absence of response to an excessive antigenic stimulus—was first described by Felton *et al.* (*J. Immunol.*, 1955, **74**, 17 and 26), whose experiments were carried out with pneumococcal polysaccharide in white mice. At the Municipal Infectious Diseases Hospital, Barcelona, the present author has studied a similar phenomenon in greater detail. Rabbits were used in hyperimmunization experiments in which suspensions of human erythrocytes of Group O and of *Brucella abortus* (Strain 19) organisms were used as corpuscular antigens and horse serum as a soluble antigen. Intravenous injections of 1 ml. of a 50% suspension of erythrocytes were given to 2 rabbits twice weekly for 7 months, after which one of them received 2 ml. daily for a further 187 days and finally 4 ml. daily for 20 days. *Br. abortus* was given intravenously as a suspension containing 2,000 to 2,500 million organisms per ml., 0·3 ml. being given 3 times weekly for 202 days and 0·6 ml. for another 182 days. Two of the 3 rabbits thus immunized received further doses of 1·8 ml. for 38 days and of 9 ml. for 7 days. Horse serum was injected intravenously into 3 rabbits 3 times weekly in increasing doses, one receiving a total of 14·969 g. of protein over a period of 550 days, another a total of 17·912 g. in 595 days, and the third a total of 0·986 g. in an unspecified period. Antibody titres to the corpuscular antigens were determined by serial agglutination with the customary double-dilution technique and those to horse serum by Ouchterlony's agar diffusion technique, again using doubling dilutions.

Haemagglutination titres were highest after 2 to 4 months and then fell steeply to between one-half and one-quarter of their peak values, remaining at the lower level in spite of continued immunization. When the immunizing dose was increased a slight rise of titre was observed, but the level then fell again and never reached the previous maximum. The titres of *Br. abortus* agglutinins rose to their peak values within 1 to 2 months and then fell steeply to between one-tenth and one-twentieth of their peak values, where they remained apart from minor temporary rises due to increased doses. The titres of precipitins against horse serum also reached their maximum values after 2 to 3 months' immunization, then falling to between one-quarter and one-twentieth of the peak value.

The author considers the phenomenon observed by him to be of a different nature from that described by Felton *et al.*, who used one single overwhelming dose of antigen so that a quantitative factor in the relationship between circulating antigen and absorbing antibodies as they were formed must have played a great part. It is postulated that under the conditions of the present investigation a state of equilibrium exists between antigenic stimulation and circulating antibodies. This state of equilibrium is not dependent on an excess of circulating antigen because the titres of the various antibodies do not fall when the dose of antigen is increased, but on the contrary show a moderate rise. The phenomenon observed may have some bearing on human desensitization and also possibly on the state of acquired immunological tolerance during the foetal and immediate postnatal periods. *K. Zinnemann*

1390. **Evaluation of the Hemagglutination Reaction as a Diagnostic Tool in Infectious Hepatitis**
J. A. MORRIS and K. NAKAMURA. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **55**, 726–732, May, 1960. 7 refs.

In view of the report by Hoyt and Morrison (*Proc. Soc. exp. Biol. N.Y.*, 1956, **93**, 547 [and also *J. Lab. clin. Med.*, 1957, **49**, 774; *Abstr. Wld Med.*, 1957, **22**, 424]) that serum from patients with infective hepatitis agglutinates the erythrocytes of the rhesus monkey, the present authors, working at the 406th Medical General Laboratory, San Francisco, have tested acetone extracts of serum for agglutinins against both monkey and chick erythrocytes. Paired sera from 20 patients with clinically diagnosed infective hepatitis contained the same titres of monkey cell haemagglutinins as sera from 20 healthy controls. With regard to chick cell haemagglutinins, of the sera from the 20 hepatitic patients 8 showed a fall in titre during the course of illness, 2 with high titres showed no change, and the remaining 10 contained no haemagglutinins at any time. In the 20 control subjects the serum of 17 at no time contained any chick haemagglutinins, whereas in that of the other 3 the factor was present at a constant level. The results of tests on paired sera from patients suffering from mumps, leptospirosis, poliomyelitis, lymphocytic choriomeningitis, and jaundice did not differ from the findings in the controls. However, sera from 6 cases of infectious mononucleosis, like many from cases of infective hepatitis, contained in the acute phase a high level of chick cell haemagglutinins which markedly diminished or disappeared completely during convalescence. It had been hoped to be possible to isolate a specific inhibitor of chick cell haemagglutinins in sera from patients convalescent from infective hepatitis, but tests designed to do so gave disappointingly negative results.

The authors point out that the unusually high frequency of monkey erythrocyte haemagglutinins observed in this study might be accounted for by small differences in technique in different laboratories. They suggest that a fall in serum levels of chick cell haemagglutinins occurring during the course of an illness may be a useful aid in the differential diagnosis of infective hepatitis, provided that infectious mononucleosis can be excluded.
*Janice Taverne*

# Pharmacology and Therapeutics

1391. **A Controlled Study of Trimethobenzamide (Tigan), a Specific Antiemetic**

A. L. KOLODNY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **239**, 682–689, June, 1960. 2 figs., 17 refs.

The author describes an investigation to determine the anti-emetic efficacy of trimethobenzamide hydrochloride (" tigan ") which was carried out, using the double-blind technique, on 161 patients with nausea and vomiting associated with infection, drug-induced allergy, hyperemesis gravidarum, and other conditions. The drug was given in a dosage of 200 mg. every 6 hours orally, intramuscularly, or by rectal suppository to 95 patients, the other 66 receiving an identical placebo by the same routes. The groups were closely similar in regard to average age (26·9 and 25·6 years respectively) and the duration of symptoms before treatment was 1 or 2 days. The patients were observed for evidence of dryness of the mouth, dizziness, changes in pulse rate and blood pressure, and rapidity of relief of symptoms after administration of the drug.

Nausea was suppressed in 58 (61%) and vomiting in 79 (83%) of the 95 treated patients; slight nausea persisted after treatment in 21. A further 32 patients receiving the drug and 12 who received the placebo experienced a decrease in the severity of the symptoms. No amelioration occurred in 5 patients receiving trimethobenzamide or in 54 receiving the placebo. Of the 5 in the treated group who failed to respond to medication 2 had virus gastritis and 3 had gastro-enteritis, alcoholic gastritis, and congestive cardiac failure respectively. The onset of relief occurred within an average period of 30 minutes after administration of the drug, and the duration of relief was 4 to 5 hours. No side-effects were observed in either group. The author concludes that trimethobenzamide is a safe and effective anti-emetic.

*Anne Tothill*

1392. **Further Studies on the Evaluation of Antitussive Agents Employing Experimentally Induced Cough in Human Subjects**

H. A. BICKERMAN and S. E. ITKIN. *Clinical Pharmacology and Therapeutics* [*Clin. Pharmacol. Ther.*] **1**, 180–191, March–April, 1960. 6 figs., 4 refs.

Experimental cough induced by the inhalation of citric acid aerosols (Bickerman *et al.*, *Amer. J. med. Sci.*, 1956, **232**, 57) was used at the Goldwater Memorial Hospital (College of Physicians and Surgeons, Columbia University), New York, in an evaluation of the antitussive activity of 13 drug preparations (including 3 placebos). The preparations were administered by mouth in random sequence to each of 16 healthy subjects and cough tests performed at hourly intervals for either 4 or 7 hours. Differences in both degree and duration of effect on the cough response as indicated by pneumotachographic tracings permitted the groupings of the preparations into three categories: (1) ineffective drugs —the 3 placebos and 9558-U (6-dimethylamino-4:4-diphenyl-3-hexanone HCl); (2) drugs with sustained antitussive activity over the 4-hour test period—morphinolinylethylmorphine (10 mg.), dihydrocodeinone resin (5 mg.), and 4964-U ($\beta$-methyl-$\alpha$, $\alpha$-diphenyl-1-piperidine ethanol HCl) (60 mg.); and (3) drugs with maximum cough suppression at the second hour and reduced effect thereafter—benzonatrate ($\omega$-methoxypoly-(ethyleneoxy)-ethyl *p*-butylaminobenzoate) (100 mg.), methadone (DL-4:4-diphenyl-6-dimethylamino-3-heptanone) (2·5 mg.), homarylamine (*N*-methylhomopiperonylamine) (20 mg.), and codeine (15 mg.). The mechanisms responsible for the differences are discussed.

*J. E. Page*

1393. **Clinical Evaluation of Benzthiazide, an Oral Diuretic**

C. W. H. HAVARD and P. H. N. WOOD. *British Medical Journal* [*Brit. med. J.*] **1**, 1773–1776, June 11, 1960. 2 figs., 12 refs.

A comparison of the diuretic properties of benzthiazide with those of chlorothiazide was carried out at St. Bartholomew's Hospital, London, on 17 patients, of whom 15 were oedematous and 2 were control subjects without oedema. Of the oedematous patients, 9 were in cardiac failure and had not previously undergone treatment with diuretics and 6 were suffering from hepatic cirrhosis. During the experimental period the food and fluid intake of the 2 control subjects was similar. Urine was collected under strictly anaerobic conditions at 2-hourly intervals for 10 hours and the urine passed in the next 14 hours was collected and pooled. Observations were made both before and after single doses of either 100 mg. of benzthiazide or 1 g. of chlorothiazide, given by mouth; 3 complete days elapsed between each experiment. The *p*H, $CO_2$ content, titratable acidity, and sodium, potassium, and chloride concentrations in the urine were measured. In the 15 oedematous patients fluid consumption was maintained at 1·5 litres and the sodium intake restricted to 25 mEq. daily. All patients were weighed daily and 24-hour collections of urine were made throughout. The trial was introduced with a 4-day control period of bed rest and one of the test diuretics was then administered for 4 days, after which a rest period of 2 to 4 days elapsed before the administration of the other diuretic for a further 4 days, the dosage of chlorothiazide being 1 g. and that of benzthiazide 100 mg. daily, both being given by mouth. Urine volume and electrolyte excretion were measured daily and serum electrolyte levels and blood urea content twice weekly.

In the 2 control subjects with both diuretics urine flow was maximal in the first 6 hours after administration and returned to normal within 10 hours. The electrolyte

excretion pattern was similar to that of water excretion but benzthiazide caused a greater loss of sodium. Chlorothiazide caused secretion of alkaline urine in the first 6 hours, but thereafter the urinary *p*H was the same as on the control days. Bicarbonate excretion was greatly increased in the first 6 hours after chlorothiazide but was unchanged after benzthiazide.

Four of the 9 patients with cardiac failure lost an average of 5·5 kg. (12 lb.) in weight during the combined periods of treatment; the remaining 5 lost only 0·7 kg. (1·5 lb.). In all cases benzthiazide caused a urinary loss of chloride in excess of that of sodium, whereas chlorothiazide caused equimolecular loss of these electrolytes. Potassium loss was of the same order for both drugs. The blood urea level was reduced in all patients. No hepatic, haematological, or gastro-intestinal disturbances were observed.

In all the cases of hepatic cirrhosis the disease was advanced and the serum albumin level low. Two patients had undergone a portal–systemic shunt operation some years previously and presented with oedema but no ascites. In one of these 2 cases treatment was associated with an increased urinary loss of sodium and chloride, with little change in potassium excretion. In the other there was no response to treatment, the blood urea level rose rapidly, and death occurred within a week. In the remaining 4 patients, whose ascites had become refractory to conservative measures so that they had been referred for portacaval anastomosis, treatment with the two diuretics resulted in a loss of weight in only 2 cases.

The results suggest that benzthiazide is an effective diuretic, 100 mg. being equivalent to 1 g. of chlorothiazide. Both drugs have the disadvantage of causing an increased excretion of potassium, but benzthiazide causes a disproportionate increase in chloride excretion compared with that of sodium. However, benzthiazide does not increase the excretion of bicarbonate as does chlorothiazide and the volume of urine excreted is greater with the former drug. *Anne Tothill*

1394. **The Diuretic Activity of Bendrofluazide**
A. C. KENNEDY, K. D. BUCHANAN, and C. CUNNINGHAM. *Lancet* [*Lancet*] **1**, 1267–1270, June 11, 1960. 3 figs., 9 refs.

An investigation of the action of the oral diuretic bendrofluazide (" aprinox "), another benzothiadiazine derivative, is here reported from the Royal Infirmary, Glasgow. It was carried out on 19 oedematous patients, of whom 14 had congestive cardiac failure, 3 hepatic cirrhosis, one the nephrotic syndrome, and one premenstrual oedema, and on 2 healthy young male subjects. To 14 oedematous patients a single dose of 5 or 7·5 mg. of the drug was given, the urine having been previously collected for a control period of 24 hours and again for two periods each of 12 hours after medication. Blood samples were also taken just before the drug was given and again 24 hours later. The samples of urine were analysed for content of sodium, chloride, potassium, and inorganic phosphorus and the volume recorded, while the blood samples were analysed for content of urea, sodium, chloride, and potassium. In a sub-group of 7 oedematous patients the serum potassium level was determined before and after several different doses of bendrofluazide, and the 2 healthy young men were given 5, 7·5, and 10 mg. of the drug at intervals of 7 days, the urine being collected on each occasion and the estimations mentioned above carried out.

A definite diuresis was obtained in 3 oedematous patients and in one normal subject given 5 mg. of bendrofluazide, and in all oedematous patients and both normal subjects when the dose was 7·5 mg. In all cases the diuresis was greatest in the first 12 hours and less in the second 12 hours. The urinary excretion of sodium, chloride, and potassium was increased, a 2-fold increase in sodium and chloride being obtained with the 5-mg. dose and a 3- to 4-fold increase with the 7·5 mg. dose. Potassium excretion was increased to a lesser extent, and the excretion of inorganic phosphorus was not significantly affected in the 13 cases studied. The plasma levels of sodium, chloride, and urea were unchanged after a single dose of bendrofluazide, but the plasma potassium level fell after a dose of 7·5 mg. No toxic effects were observed in any case. It is concluded that bendrofluazide, in the optimum dose of 7·5 mg., acts as an osmotic diuretic, causes a powerful excretion of sodium and chloride, and does not give rise to hypokalaemia.
*Anne Tothill*

1395. **The Hypotensive Action of Diuretic Agents**
E. G. MCQUEEN and R. B. I. MORRISON. *Lancet* [*Lancet*] **1**, 1209–1212, June 4, 1960. 5 figs., 31 refs.

In a study carried out at the University of Otago, Dunedin, New Zealand, the relationship between the diuretic and hypotensive actions of chlorothiazide and hydrochlorothiazide were compared with those of mersalyl in non-oedematous hypertensive patients who showed no evidence of heart failure and were on a free diet, with uncontrolled sodium and fluid intake. During the control period, the patients received placebo tablets and were familiarized with the method of multiple recording of blood pressure, and three 24-hour samples of urine were collected. The diuretic was then given for 3 days, during which further 24-hour urinary samples were collected. Chlorothiazide was given to 16 patients in a dosage of 0·5 g. twice daily, hydrochlorothiazide (50 mg. twice daily) to 30 patients, and mersalyl (2 ml. daily) to 16 patients.

The three diurectics produced equivalent hypotensive responses, the fall in blood pressure corresponding to the amount of water and sodium excreted. The plasma volume was also reduced and its restoration by means of infusion of salt-free dextran also restored the blood pressure to its pre-treatment level. *Norval Taylor*

1396. **A Rapid Quantitative Method for the Comparison of Diuretic Agents in Bed-patients with Congestive Failure**
H. GOLD, N. T. KWIT, A. J. GOLFINOS, and I. D. J. BROSS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **239**, 665–681, June, 1960. 3 figs., 16 refs.

A technique for the evaluation of diuretic agents during the routine treatment of cardiac failure is described in this paper from Cornell University Medical

College and three New York hospitals. It is claimed that a rapid assessment of diuretic effect is possible with comparatively few patients by this method, in which the agent under test is assayed against a "standard" agent in the same patients. The two diuretics (A and B) are administered in doses giving a maximal response on 4 successive days, the order being ABBA and BAAB in alternate cases. The diuretic response to each dose is assessed by measuring the loss of weight in the next 24 hours. The efficacy of the test drug in relation to that of the standard is then computed "from the ratios of the measured responses in a group of patients, and from an analysis based on signs with the sign test for the reliability of the answer".

In a number of tests of the reliability of the method the patients received a standard regimen of treatment for heart failure throughout. The diet contained 2 g. of sodium daily, often given as 1·5 litre of water and 1·5 litre of milk, and digitalis was prescribed. The standard diuretic used was meralluride in a dose of 2 ml. injected intramuscularly. Consistent results were obtained when meralluride was also used as the test drug in the same dosage in 20 patients. When 1 ml. of meralluride was compared with the standard in 9 patients the response to the former was 61·6% of that to the latter. Chlorothiazide in a dose of 2 g. given by mouth to 7 patients produced 47·2% and 1 g. of an experimental phenothiazine compound given by mouth to 8 patients produced 47·3% of the response to 2 ml. of meralluride intramuscularly. *David Phear*

1397. **Comparison of Chlorothiazide and Meralluride: New Rapid Method for Quantitative Evaluation of Diuretics in Bed-patients in Congestive Heart Failure**
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Chlorothiazide in doses of 2 g. by mouth produced an average maximum diuretic response equivalent to 40% of the response to 2 ml. of meralluride injected intramuscularly or 70% of that to 1 ml. of meralluride. Clearing of oedema took 2½ times longer with chlorothiazide than with meralluride. *David Phear*

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In a clinical trial carried out at Harlem Hospital, New York, methyprylone ("noludar"), a piperidine derivative was given as a sedative hypnotic to 1,131 adult patients, of whom 885 had functional disturbances associated with organic disease and 246 had emotional disturbances only. The dose used was 50 mg. four times a day, but in 14 cases this had to be reduced to twice a day as the patient became unduly drowsy. In 93% of these cases relief of tension was reported. In addition 25 patients with insomnia were given 300 mg. of methyprylone at night; in 22 cases a good night's sleep was obtained. Studies with radioactive iodine showed that the drug had no effect on iodine uptake, nor were there any other side-effects except drowsiness.

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allow for individual variations in response. The subjects were told something of the nature of the drug, but were not told what results might be expected, nor did they know whether they were receiving the drug or the placebo. After 6 weeks the double-blind test was concluded and all 35 subjects were given deanol for a further 6 weeks.

Neither the placebo nor the drug produced any change in systolic or diastolic blood pressure, heart rate, muscle power, hand steadiness, vital capacity, or body weight, while the serum cholesterol and protein-bound iodine levels, gastric acid content, and the cephalin–cholesterol flocculation reaction were all unaffected. At the end of each week the subjects filled in a questionary concerning the subjective effects of the drugs. Statistical analysis of the replies revealed that there was a significant improvement in mental concentration and muscle tone among the subjects taking deanol, some of whom also noted that sleep was sounder and that less was required. Most of these changes were recorded at the end of the second week, when the subjects had been taking a daily dose of 20 mg. of the drug. *P. A. Nasmyth*

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The effects of glutethimide, a non-barbiturate hypnotic, were studied in 16 young volunteers at Georgetown University Medical Center, Washington, D.C. The drug was dissolved in polyethylene glycol 400 and administered intravenously in doses of up to 2 g.; the electroencephalogram and electrocardiogram were recorded before, during, and after injection of the drug, and the respiratory changes also recorded.

The rapid injection of 1 to 2 g. of glutethimide produced loss of consciousness and a short period of skin analgesia, the injection being accompanied by discomfort or burning pain radiating up the arm. There was no appreciable depression of pulmonary ventilation except for respiratory arrest for a brief period in 2 of the subjects and there were no significant changes in the blood pressure. The drug exerted a general parasympatholytic effect. Recovery of consciousness was rapid; in a few cases the intravenous administration of bemegride successfully shortened the time before ambulation became possible. There was marked variation in the degree of effect produced by glutethimide in different patients and a lack of correlation between blood level of the drug and clinical state. *Mark Swerdlow*

1402. **Intravenous Nonbarbiturate, Nonnarcotic Analgesics: Preliminary Studies. I. Cyclohexylamines**

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CI 400, which was claimed to be largely devoid of these undesirable effects, was administered to 29 unpremedicated patients about to undergo dilatation and curettage in doses ranging from 0·15 to 0·25 mg. per kg. body weight. Soon after injection a state of catatonia developed followed by generalized rigidity without myoclonic movements which, when sensory blockade was established, gave way to "plastic stiffness". Three minutes after injection the patient did not respond to her name and after 5 minutes sensory blockade was complete and surgery could be performed. However, this state was achieved in less than half the patients, and in the remainder marked agitation and hallucinations occurred. The pulse rate and blood pressure showed rises of about 35%, but there were no electrocardiographic abnormalities. The rate and depth of respiration increased in all patients. The state of catatonic rigidity subsided in most patients in about 10 minutes. By the end of 15 to 20 minutes most patients could respond to commands, and after 30 minutes blurred speech was present. Drowsiness, blurring of vision, and incoordination, however, persisted for one to 4 hours. These side-effects impair the therapeutic value of the drugs, but it is hoped that analogues of the cyclohexylamines may be found which do not produce such undesirable reactions. *Mark Swerdlow*

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College and three New York hospitals. It is claimed that a rapid assessment of diuretic effect is possible with comparatively few patients by this method, in which the agent under test is assayed against a " standard " agent in the same patients. The two diuretics (A and B) are administered in doses giving a maximal response on 4 successive days, the order being ABBA and BAAB in alternate cases. The diuretic response to each dose is assessed by measuring the loss of weight in the next 24 hours. The efficacy of the test drug in relation to that of the standard is then computed " from the ratios of the measured responses in a group of patients, and from an analysis based on signs with the sign test for the reliability of the answer ".

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# Infectious Diseases

1404. **Mumps Virus Infection Simulating Paralytic Poliomyelitis**
E. H. Lennette, G. E. Caplan, and R. L. Magoffin. *Pediatrics* [*Pediatrics*] **25**, 788–797, May, 1960. 18 refs.

During an investigation into the virus aetiology of diseases of the central nervous system an opportunity occurred to study a number of cases clinically regarded as of paralytic poliomyelitis but which, for various reasons, did not appear to be due to infection with poliomyelitis virus. In this paper from the California State Department of Public Health, Berkeley, 11 cases are reported in which the presenting symptoms were fever, nuchal rigidity and stiffness of the back, muscle pains, and slight to moderate muscle weakness. In all the cases there was definite serological evidence of mumps virus infection but no evidence of poliomyelitis infection. The cerebrospinal fluid contained 100 to 300 lymphocytes per c.mm. Electroencephalography was carried out in 8 cases and in 3 of these the tracing was abnormal. Evidence of parotitis was found in only 2 cases. All the patients had muscle weakness during the acute phase of the disease and slight weakness persisted in 4 during convalescence. No particular muscle group was affected. *Winston Turner*

1405. **Inoculation Hepatitis Associated with Anti-measles Serum.** (Инокуляционный гепатит, связанный с введением противокоревой сыворотки)
I. N. Rudenskaja. *Вопросы Охраны Материнства и Детства* [*Vop. Ohrany Materin. Dets.*] **5**, 31–35, May–June, 1960. 13 refs.

The author describes an outbreak of virus hepatitis which occurred in the Komi region of the U.S.S.R. during February and March, 1959, among a number of children who had received prophylactic injections of anti-measles serum of a particular batch. No children receiving serum of other batches or those not inoculated contracted the disease, but 41% of those receiving this particular batch did so, and of these 60% were under 3 years of age; in 40% of the cases the disease was severe and the mortality high (15%). The average incubation period was 75 days (range 40 to 133 days). Contrary to the reports of previous authors, there was no relationship between length of incubation and severity, except that 5 children with an incubation period of over 100 days were very mildly affected and did not develop jaundice.

Clinically the disease did not differ, apart from the high proportion of severe cases, from the usual type of infective hepatitis. Of the affected children 7 suffered short relapses in the course of the illness, but none had late relapses or developed chronic hepatitis. The severity of the attack was not associated with the state of the child's nutrition or with the fact of its having developed measles or not in the interval between inoculation and the onset of hepatitis. These children had all received gamma-globulin in addition to anti-measles serum, but this did not appear to have decreased the liability to hepatitis, since the incidence of this complication was higher than that in previously reported outbreaks in which gamma-globulin had not been given. In only one case was there any question of transmission to another child, one girl developing fatal hepatitis 54 days after her brother had been admitted to hospital for inoculation hepatitis (also with fatal outcome). The mothers of 2 children suffering from inoculation hepatitis also developed the disease, but in these cases infection may have been transmitted from cases of enteral virus hepatitis while the mothers were in the hospital with their children. *L. Firman-Edwards*

1406. **Glucolytic Enzymes in the Serum of Children Suffering from Infective Hepatitis.** (Некоторые ферменты гликолиза в сыворотке крови детей страдающих болезнью Боткина)
R. F. Ezerskij. *Вопросы Охраны Материнства и Детства* [*Vop. Ohrany Materin. Dets.*] **5**, 40–43, May–June, 1960. 2 figs., 9 refs.

In this study the clinical progress of infective hepatitis (Botkin's disease) was correlated with the changes in aldolase and phospho-glucose isomerase activity in the serum of 58 children with the disease and 20 controls. Activity of the former enzyme was estimated by the method of Tovarnitskii and Voluiskaya and that of the latter by the method of Bodansky and Bruns. The changes in isomerase levels bore a closer relation to the clinical progress than did those of aldolase and the technique of determining the former is simpler. The normal isomerase level is given as 1 to 5 units [but Jegatheesan and Joplin (*Proc. roy. Soc. Med.*, 1960, **53**, 3) reported the normal maximum as 25 units]. In the milder cases the fall in isomerase level was continuous, but in the more severe cases there was a tendency to a slight rise after the second week, while the serum bilirubin level fell until the third week and then remained constant at around 1·5 mg. per 100 ml. The author suggests that from the dynamic changes in the levels of these glucolytic enzymes it is possible to judge of the severity of the hepatic involvement.

*L. Firman-Edwards*

1407. **Natural History of 338 Treated and Untreated Patients with Staphylococcal Septicaemia (1936–1955)**
I. M. Smith and A. B. Vickers. *Lancet* [*Lancet*] **1**, 1318–1322, June 18, 1960. 4 figs., 26 refs.

A review carried out at the University Hospitals and State University of Iowa, Iowa City, of the clinical and necropsy records of 338 cases of staphylococcal septicaemia occurring in the period 1936–55 showed that in 69 cases the infection had supervened during the course

of a fatal illness such as malignant tumour. Patients aged less than 10 years or more than 69 years formed 35·5% of the series. The ratio of males to females was 1·94 to 1, with corresponding fatality rates of 75·3 and 81%. The months of highest incidence were November, January, March, and April. A statistically significant decline in mortality occurred during the years 1952–5.

Bacteriological investigation revealed that in the majority of cases the infecting organism was *Staphylococcus aureus*. Although the skin was an important focus of infection in patients with primary septicaemia, infections originating in the respiratory tract or after surgical intervention were associated with a higher death rate. The authors state that " a distressing number of infections were acquired in hospital " and suggest that transoral or transnasal catheter suction may have led to severe pneumonia in nasal carriers of hospital staphylococci. A maximum leucocyte count of more than 20,000 per c.mm. was a bad prognostic sign. Endocarditis was detected in 10% of cases with staphylococci in the blood-stream. Haemorrhagic necrotizing pneumonia was a common finding at necropsy, and multiple abscesses were also often encountered, especially in the kidneys. During the period 1936–40 antimicrobial drugs were employed in only 21% of cases, but between 1941 and 1955 most patients received these drugs. It was noted that mortality decreased as each new drug was introduced, but these new agents lost their efficacy with continued use. The fatality rate was relatively low among patients given combined penicillin and sulphonamide therapy.

The authors point out that, in view of the increasing proportion of aged and debilitated patients in hospital, prevention of cross-infection becomes of particular urgency, especially when adrenal steroid therapy is employed. A series of three blood cultures should suffice for diagnostic purposes. They conclude that provided the diagnosis is correct and that the antibiotic sensitivity of the strain is known the fatality rate should not exceed 25%. *A. Garland*

1408. **Combined Phenylbutazone and Tetracycline in the Treatment of Typhoid Fever**

F. Ruiz Sánchez and E. Naranjo Granda. *Antibiotic Medicine and Clinical Therapy* [*Antibiot. Med.*] **6**, 537–544, Sept., 1959 [received May, 1960]. 3 figs., 13 refs.

At the Civil Hospital, Guadalajara, Mexico, satisfactory results had previously been obtained in treating typhoid fever with a combination of phenylbutazone and chloramphenicol.

In the present study 18 patients suffering from typhoid fever, 11 males and 7 females aged between 5 and 38 years, were treated with a combination of phenylbutazone and tetracycline with citric acid (" achromycin V "). The dosage of phenylbutazone was 300 to 1,200 mg. daily and of tetracycline 50 mg. per kg. body weight per day. The results are reported as " very good " in 15 (83·3%) of the patients, in whom the fever was controlled within 36 hours. In 2 patients treated with tetracycline alone as a control the results are described as " unsatisfactory ". *John Fry*

1409. **Treatment of Tetanus with Acetylpromazine**

R. Wright. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. med. Hyg.*] **54**, 270–273, May, 1960. 12 refs.

From King Edward VIII Hospital, Durban, the author describes the use of the phenothiazine derivative acetylpromazine in the treatment of 33 cases of tetanus, 25 neonatal and 8 non-neonatal. Initially the drug was given alone in high dosage in 3 very severe cases of the 25 of tetanus neonatorum, but the treatment failed to control the spasms and the infants died within 24 hours. Subsequently, in view of the known potentiation of barbiturates by phenothiazine derivatives, the drug was combined with phenobarbitone sodium and recovery was obtained in 3 of the 22 infants so treated. In many of the fatal cases, although the spasms were controlled within 48 hours, the infants became flaccid and died from respiratory failure. The treatment regimen was as follows. While the spasms were severe 10 mg. of acetylpromazine was administered together with 30 mg. of phenobarbitone sodium, 2 to 4 times daily. For the 8 older patients the first dose of acetylpromazine ranged from 10 to 50 mg. according to the frequency and severity of the spasms, this being followed by 20 to 25 mg. or more every 4 to 6 hours, phenobarbitone being sometimes added to control the spasms. With this treatment 5 of the 8 patients recovered.

The author states that there was little doubt concerning the value of acetylpromazine in relieving spasms and removing muscle rigidity, for neither tube nor intravenous feeding was required by those patients who recovered. In regard to toxic symptoms, confusion, hallucinations, and incontinence developed in one male patient aged 19 after a total dosage of 2,140 mg. of acetylpromazine, while slight hypotension and tachycardia were side-effects in other cases. Discussing his previous experience with chlorpromazine the author points out that acetylpromazine has 5 to 10 times the antitetanic effect of the latter. Respiratory failure particularly in neonatal infants is a constant hazard, however, and in this context it is hoped to pursue investigations into the use of neuromuscular block and intermittent positive-pressure respiration. *A. Garland*

1410. **Excessive Perinatal Mortality in a Small Town Associated with Evidence of Toxoplasmosis**

J. S. Robertson. *British Medical Journal* [*Brit. med. J.*] **2**, 91–96, July 9, 1960. 1 fig., 20 refs.

Significant differences in perinatal mortality among three areas of Lincolnshire over a 3-year period are shown to be due to variation in stillbirth rate. Investigation of possible causes of this showed that there was a significantly higher incidence of cytoplasm-modifying antibody to *Toxoplasma gondii* in the women whose babies had been stillborn, when compared with a group of mothers who had been delivered of live babies in the same month and in the same place. The two groups did not differ greatly in age, parity, or in any other respect. The hypothesis that toxoplasmosis may have been the cause of these stillbirths is discussed.—[Author's summary.]

# Tuberculosis

1411. **The Treatment of Juvenile Tuberculosis with Tebafen (GT3).** (Über die Behandlung kindlicher Tuberkuloseformen mit Tebafen (GT3))
H. W. KIRCHHOFF. *Schweizerische Zeitschrift für Tuberkulose und Pneumonologie* [*Schweiz. Z. Tuberk.*] **17**, 93–116, 1960. 6 figs., 19 refs.

This paper from the Children's Clinic of Saar University records the experience accumulated since 1954 in the treatment of 392 children, aged from 3 months to 14 years, who were suffering from various forms of primary tuberculosis and who were given "tebafen", a combination of isoniazid and thiosemicarbazone (thiacetazone).

The dosage of 5 to 10 mg. per kg. body weight was well tolerated and the results were generally favourable. Thus haematogenous or bronchogenic spread was prevented; hilar lymph nodes were not, as reported in other forms of treatment, particularly affected: reduction of hilar adenopathy was observed radiologically in 45 cases, in 36 others there was temporary enlargement followed by later clearing, while in 102 cases the process remained stationary. *A. J. Karlish*

1412. **Mass Chemoprophylaxis of Tuberculosis. The Acceptability and Untoward Side Effects of Isoniazid in a Control Study in Greenland**
E. GROTH-PETERSEN, U. GAD, and F. ØSTERGAARD. *American Review of Respiratory Diseases* [*Amer. Rev. resp. Dis.*] **81**, 643–652, May, 1960. 1 fig., 17 refs.

A large-scale controlled study of the potential value of isoniazid in the chemoprophylaxis of tuberculosis in adults was started among the general population of Greenland in the summer of 1956. The present paper from the Danish Tuberculosis Index, Copenhagen, and Dronning Ingrids Sanatorium, Godthaab, Greenland, presents observations on the acceptability of prophylactic medication by a population of presumably healthy adults and on the side-effects of isoniazid. The long-term effect on morbidity cannot yet be assessed.

The entire native population of West Greenland aged 14 years and over, except for those living in the smallest and most remote villages, was included in the trial, the participants numbering 10,112 (84·7% of the total adult population) and inhabiting 79 villages. Children were excluded because it was considered too risky to prescribe different doses to different persons in the same village; moreover, most of the children had received B.C.G. vaccination. All participants were required to submit to radiographic examination of the chest, the films being read independently by two radiologists, and sputum examination was included as a routine measure. Persons with active tuberculosis were excluded. The participating villages were arranged in order according to the number of adult inhabitants and by random selection one of every two successive villages was assigned to isoniazid treatment and the other to placebo treatment. The numbers of persons receiving isoniazid and placebo were thus approximately equal, though their identity was known to 2 persons only, both in Copenhagen. The dose of isoniazid was 400 mg. or, in some cases, 600 mg. given in 2 or 3 pills on two successive days each week. No added vitamins were given. "For tactical reasons" the placebo pills each contained 0·1 mg. of isoniazid, together with 2 mg. of quinine sulphate to give them a bitter taste like that of isoniazid. Both groups were treated for two periods of 13 weeks separated by an interval of 13 weeks. Only 1·3% of the population of the area studied failed to participate and subsequent defaulters amounted to 4·8% of those entering the trial.

The participants were deliberately not questioned about special symptoms. There were, however, various spontaneous complaints from 1·1% of the isoniazid group and from 1·3% of the placebo group. In no case were serious side-effects observed, nor were complaints more frequent from those receiving 600 mg. than from those receiving 400 mg. of isoniazid. At the same time the authors state that there are several indications that side-effects may actually have been more frequent in the isoniazid group and that they differed in some respects from those in the placebo group. No evaluation can yet be made of the potential harm caused by the development of isoniazid-resistant bacilli in comparison with the potential benefit of prophylaxis in reducing tuberculosis morbidity.

[This is an exceptionally interesting account of a survey carried out under rigorous conditions.]

*Norman F. Smith*

1413. **Experience in Tracing Sources of Infection of Tuberculin Converters**
D. VAN ZWANENBERG. *Tubercle* [*Tubercle* (*Lond.*)] **41**, 171–177, June, 1960. 13 refs.

Writing from the Chest Clinic, St. Helen's Hospital, Ipswich, the author describes the use of a tuberculin index which was established for all tuberculin-tested children in Ipswich and East Suffolk, and which was compiled from school surveys, examination of contacts at the chest clinic, and children in hospital. Up to July, 1958, by reference to this index 109 children whose tuberculin reaction converted from negative to positive were discovered, but in only 95 was it possible to investigate the cause of the conversion. Of 31 of these cases (designated as "explained converters") the probable source of infection in 28 cases was traced to 23 individuals, of whom 16 were already known to the clinic, and the other 7 were identified on examination of the children's contacts; the remaining 3 "explained" cases were traced to the milk supply. That the use of the index failed to trace the sources in most cases is disappointing and the author suggests that there must be much chance infection outside the household, for example in public places and buses. It is noted that more sources of infection were found when the tuberculin conversion

had taken place recently or when all the children in a household were tuberculin positive. Of the 95 children discovered in this survey who converted 7 developed definite tuberculous disease. *Paul B. Woolley*

1414. **The Treatment of Pulmonary Tuberculosis at Work: a Controlled Trial**

REPORT FROM THE RESEARCH COMMITTEE OF THE TUBERCULOSIS SOCIETY OF SCOTLAND. *Tubercle* [*Tubercle (Lond.)*] **41**, 161–170, June, 1960. 3 figs., 18 refs.

In view of the striking success of chemotherapy in recent years in the treatment of pulmonary tuberculosis many physicians have come to doubt if bed rest in addition is an essential curative factor. This paper deals with a total of 103 tuberculous patients who were selected according to an agreed protocol by individual physicians at 11 centres in Scotland and divided at random into two groups: (1) 49 who in addition to chemotherapy were kept at rest in bed, and (2) 54 who were allowed to continue at work. The sputum of all the patients was initially negative on direct smear or concentrate examination, but in about half the cases gave a positive culture, and the disease was of only minimal or moderate extent, in none being " far advanced ". Both groups received the same drug treatment, namely, 5 g. of sodium PAS and 100 mg. of isoniazid twice daily for a period of 6 months. The patients underwent periodic sputum and x-ray examinations, when the weight was also recorded, and the erythrocyte sedimentation rate determined.

At the end of 3 months (the minimum period of bed rest) it was found that those who had continued to work did at least as well as those who had bed rest and in some respects slightly better. At the end of 2 years 6 patients (2 in the bed rest and 4 in the work group) had deteriorated, but in 5 of these there was good evidence that this was due to neglecting their chemotherapy. This is of course more likely to occur in those who are allowed to continue working. The authors conclude from this and other reported studies that patients with slight active tuberculous disease may be allowed to continue their occupation provided they can be relied on to take their drugs regularly, but that such treatment should not be undertaken lightly. *Paul B. Woolley*

1415. **New Stick Test for P.A.S. in Urine: Report on Use of " Phenistix " and Problems of Long-term Chemotherapy for Tuberculosis**

G. R. W. N. LUNTZ and R. AUSTIN. *British Medical Journal* [*Brit. med. J.*] **1**, 1679–1684, June 4, 1960. 26 refs.

" Phenistix " strips are paper sticks impregnated with a mixture containing ferric and magnesium salts plus *cyclo*hexyl sulphaminic acid. The strip remains yellow in normal urine, but becomes green in the presence of phenylpyruvic acid and pink or purple when the urine contains *p*-aminosalicylic acid (PAS).

On the basis of their findings in experimental tests of specificity and sensitivity and in extensive clinical trials on patients in hospital and attending chest clinics who were under treatment the authors conclude that, though not absolutely specific for PAS the phenistix test gives a good indication as to whether or not a tuberculous patient is taking his medicine. False positive results may occur if the patient is taking aspirin. *J. Robertson Sinton*

1416. **Tuberculosis Peritonitis: a Study of Forty-seven Proved Cases Encountered by a General Medical Unit in Twenty-five Years**

W. R. BURACK and R. M. HOLLISTER. *American Journal of Medicine* [*Amer. J. Med.*] **28**, 510–523, April, 1960. 8 figs., 17 refs.

Over a 25-year period 47 proved cases of tuberculous peritonitis were seen at the Boston City Hospital, Massachusetts, and in this paper the clinical and laboratory findings in these cases and the incidence of the disease are analysed. Of the 47 patients (26 male and 21 female) 20 had cirrhosis of the liver. There were 33 deaths during the period, and the findings at necropsy (27 cases) included widespread miliary tuberculosis in 12, involvement of the intestinal mucosa in 4, and genital tuberculosis in one. Abdominal swelling (29 patients) and abdominal pain (21) were the commonest symptoms. All the patients had fever at some time during the illness. In 28 there were abnormal physical findings in the lungs, including evidence of pleural effusion and/or upper lobe signs suggestive of tuberculosis. In a similar number there was " a suspicion of free abdominal fluid ", and in all except 7 overt ascites eventually developed. A " doughy " abdomen was found only in 2 cases, and was considered to be an unreliable sign of tuberculous peritonitis; characteristically in this series the abdomen was distended and drum-like. Abdominal tenderness was present in 24 patients; in 7 the right upper quadrant was tender. The liver was palpable in 20 patients, including 11 alcoholics.

Of a group of 75 patients with cirrhosis and ascites without peritoneal tuberculosis, only 6 had abdominal pain not accounted for by other complications, and it was rarely the chief complaint; in 26 there was abdominal tenderness, usually in the right upper quadrant over an enlarged liver.

Chest radiographs were available in 40 of the 47 cases of tuberculous peritonitis. Of these, 14 were normal and 4, which were initially normal, later showed apical disease; the findings in the remainder were infiltration in 14, effusions in 3, and non-specific abnormalities in 5. The specific gravity of the ascitic fluid was highest (1·020) in cases of uncomplicated tuberculous peritonitis and lowest (1·002) in those with co-existing cirrhosis. In patients with uncomplicated cirrhosis the protein concentration of the ascitic fluid was less than 2·5 g. per 100 ml., whereas in most of those with tuberculous peritonitis the value was higher. The total leucocyte count of the fluid in the former group was less than 250 per c.mm.; it was above this figure in more than half the patients in the latter group. A differential count showed that the ascitic fluid from the tuberculous patients never contained more than 20% polymorphonuclear leucocytes. The authors state that nearly one in every 3 ascitic fluid inoculations into guinea-pigs proved negative for tuberculosis and more than half the cultures examined were also negative. *B. Golberg*

# Venereal Diseases

1417. **Results of Treatment of Primary and Secondary Syphilis by a Single Injection of Slowly Released Depot Penicillin.** (Résultats du traitement de la syphilis primo-secondaire par l'injection unique de pénicilline retard à long terme)

P. DE GRACIANSKY and C. GRUPPER. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **36**, 1441–1450, May 18, 1960. 8 figs., 4 refs.

At the Hôpital St.-Louis, Paris, the authors have sought to reduce the treatment of primary and secondary syphilis to a single injection of a penicillin preparation with a sufficiently prolonged action. Since 1952 they have treated 147 patients in this way, 3 mega units of P.A.M. being given in 15 cases, 2·4 mega units of " panbiotic " or " extencilline bipenicillin " in 56 cases, and 2·4 mega units of extencilline or benzathine penicillin in 76 cases. As no differences appeared between the effects of these preparations the results in all three groups are presented together. In all cases corticosteroids were given before the penicillin to prevent a Herxheimer reaction, the dosage being equivalent to 30 mg. of prednisone each day for 5 days. The observations made included the changes in clinical signs, the rapidity of disappearance of treponemes, and the serological reactions, four separate standard tests (S.T.S.) and the treponemal immobilization (T.P.I.) test being performed. The cerebrospinal fluid (C.S.F.) was examined before treatment and again 2 years later. Fifteen of the patients were excluded from the analysis of results because of an insufficient period of observation or because they had received additional treatment by other doctors alarmed by persistent positive serological reactions. Eight patients were treated again for reinfections, 2 having actually achieved 2 reinfections. The period of observation varied from one year (12 cases) to 7 years (4 cases).

Of 11 patients treated for seronegative primary syphilis, 9 were adequately followed up, in all of whom treatment was successful. Of 57 patients with seropositive primary syphilis, 48 were observed for one year or more. In 43 cases the serology became negative and remained so, while 5 patients never became seronegative, but gave low-titre positive reactions. The T.P.I. reaction before treatment was reported as negative in 15 cases (31·3%), doubtful in 16 (35·4%), and positive in 17 (35·4%). After treatment the reaction remained negative in all of the first group, became negative within 6 months in all of the second group, and became negative in less than one year in 12 cases in the third group.

Of 79 patients with secondary (seropositive) syphilis, 75 were followed up successfully. The results of the S.T.S. became negative in 60 cases and remained positive, but in low titre, in 15; one patient only achieved this status after 4 years. The T.P.I. reaction became negative in 33 (47·8%), remained doubtful in one (1·5%), and remained positive in 35 (50·7%) of the 69 cases in which the test was repeated after treatment. No abnormality of the C.S.F. was found in these patients. Nine women treated for secondary syphilis became pregnant during the observation period and all their children were healthy. In a few cases temporary positive S.T.S. reactions appeared, without clinical signs and without a positive T.P.I. reaction, but reverted to negative within 3 months. The authors consider the results of treatment with a single dose of 2·4 mega units of penicillin in a slow-absorption form to be eminently successful.

*Robert Lees*

1418. **Surface Manifestations of Reiter's Disease in the Male**

J. A. H. HANCOCK. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **36**, 36–39, March [received May], 1960. 13 figs., 4 refs.

A detailed study is reported of the surface manifestations in 76 cases of Reiter's disease in males seen at the Whitechapel [Venereal Diseases] Clinic of the London Hospital. It is pointed out that the clinical material was partly selected in that some of the more severely ill patients were referred for forms of treatment which were not at that time available elsewhere. Involvement of the eyes was encountered in 45%, conjunctivitis being present in 37% and anterior uveitis in 8%; balanitis circinata was observed in 26%, lesions of the buccal cavity in 10%, and keratoderma blennorrhagica in 7·8%. The vesicular and erythematous lesions of the tongue and buccal cavity are described in detail [with some excellent colour plates] as are also the lesions of keratoderma and balanitis. All but 2 patients in the series (with non-gonococcal urethritis, buccal lesions, and keratoderma) exhibited arthritis. *R. R. Willcox*

1419. **Diagnosis and Treatment of Trichomonal Urethritis in Men**

R. D. CATTERALL. *British Medical Journal* [*Brit. med. J.*] **2**, 113–115, July 9, 1960. 14 refs.

The symptoms and signs in 126 cases of trichomonal urethritis in men attending the Whitechapel Clinic of the London Hospital are reviewed. Eighteen patients had no genito-urinary symptoms; in the others the most common complaint was of urethral discharge, sometimes with itching inside the penis. The combination of examination of wet urethral smears and cultures is recommended for diagnosis and follow-up. In the author's experience the most satisfactory method of treatment is by urethrovesical irrigation with a weak solution of potassium permanganate, oxycyanide of mercury, or dequalinium chloride. Amongst various groups of patients treated by irrigation with different agents the lowest cure rate was about 60%. Urethral stricture was found in 10 patients, all of whom showed a marked tendency to relapse, but the results of treatment improved after dilatation of the strictures.

*G. W. Csonka*

# Tropical Diseases

1420. **The Pathogenesis of Anhidrotic Asthenia. An Aspect of Heat Intolerance**
J. P. O'BRIEN. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **54**, 235–241, May, 1960. 2 figs., 25 refs.

Writing from the University of Sydney, New South Wales, the author describes the symptoms and discusses the mechanism of anhidrotic asthenia, a heat disorder first noted among the troops in the war of 1939–45. It takes the form of heat exhaustion characterized by absence of sweating, a peculiar rash, asthenia, and a rise in temperature. The rash (recently termed miliaria profunda) is due to blockage of the ducts of the sweat glands. The accumulated sweat distends the coil glands in the corium and may later be extravasated under the superficial layers of the epidermis, leading to miliaria crystallina; this is more likely to occur after sunburn, when the superficial layer is already becoming detached. The rash affects mainly the covered parts of the body and the face is never affected, so that a wet face, dry body, and asthenia are characteristic features of the syndrome.

Experimentally it can be shown that the anhidrosis is due to local obstruction rather than to any central defect. The author describes (and illustrates) the effect of applying lanolin locally on the skin. In the treated patch the pores of the sweat glands remain open. Similarly it can be shown that desquamation, even when caused by sunburn, prevents anhidrosis, presumably by keeping the pores open. It is probable that infection, particularly by staphylococci and monilia, may play some part in obstructing the sweat glands. An endocrine factor may be involved in the polyuria which is present in some cases, but this is more likely to be the result rather than the cause of the anhidrosis. The author considers that the origin of the condition is peripheral, and is due to mechanical blocking of the sweat glands, initiated by miliaria rubra (prickly heat). He concludes: " whatever causes miliaria rubra is therefore the cause of miliaria profunda ". *William Hughes*

1421. **Observations on the Capability of Freshwater Vector Snails to Survive Dry Conditions**
C. J. SHIFF. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **63**, 89–93, April, 1960. 10 refs.

It has been shown that if the treatment of waters with molluscides is carried out at the height of the dry season, when most rivulets have dried up, it may not prove to be successful.

Experiments were therefore carried out at the Malaria and Bilharzia Research Laboratory, Salisbury, S. Rhodesia, on the survival of three major vector snails, *Biomphalaria pfeifferi*, *Bulinus* (*Physopsis*) *globosus*, and *Lymnaea natalensis* under varying conditions of dryness, temperature, and relative humidity both in and out of doors. These showed that the first two snails could survive in damp mud for 30 to 50 days if protected from direct sunlight. *L. natalensis* was less well adapted to dryness, but could deposit viable eggs for up to 20 days under similar conditions. It is concluded that if a molluscide is applied when most of the water has dried up, many snails will not come into contact with it and will remain alive to repopulate the stream when it is replenished by rain. *Clement C. Chesterman*

## NUTRITIONAL AND METABOLIC DISORDERS

1422. **The Effect of Folic Acid on the Steatorrhea of Tropical Sprue and Other Tests for Intestinal Absorption**
R. RODRIGUEZ-MOLINA, M. CANCIO, and C. F. ASENJO. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **9**, 308–314, May [received July], 1960. 2 figs., 15 refs.

The effect of administration of folic acid in the treatment of tropical sprue was studied in 12 male Puerto Ricans, who were given 15 mg. of the drug daily (by mouth in 11 and by intramuscular injection in one) over periods varying from 9 to 44 days. Clinical improvement was noted in 11 of the 12 patients, and there was some improvement in vitamin-A absorption in 4. No striking change was observed in the results of the glucose tolerance test or the D-xylose excretion test. In 5 patients the steatorrhoea became more severe during treatment; in the remainder there was no significant change.

[Persistent steatorrhoea in patients with tropical sprue receiving folic acid treatment has been described by Frazer who attributed it to changes in the intestinal flora, since under these conditions the steatorrhoea usually responds to antibacterial therapy. (Frazer, A. C., *World Congress of Gastroenterology*, 1958, **1**, 624.)] *R. Schneider*

1423. **Nitrogen Metabolism in Children with Kwashiorkor Receiving Milk and Vegetable Diets**
J. D. L. HANSEN, H. E. SCHENDEL, J. A. WILKINS, and J. F. BROCK. *Pediatrics* [*Pediatrics*] **25**, 258–282, Feb., 1960. 8 figs., 42 refs.

This study of nitrogen metabolism in kwashiorkor was carried out at the University of Cape Town on 43 children aged between 7 months and 3 years admitted to the Red Cross War Memorial Children's Hospital with frank signs of the syndrome and grossly underweight. Each child received penicillin and sulphadiazine during the first week after admission and the efficacy of the following four diets was then tested. (1) Skimmed milk plus sugar for 2 weeks, followed by milk plus a cereal, usually maize meal. (2) Maize meal (mealie meal) supplemented with (*a*) sugar with or without

glycine, or (*b*) with egg or milk and sugar. (3) A " three component vegetable mix " consisting of maize meal, maize germ, and cow pea meal (*Pisum sativum*) in equal parts, with added sugar. (4) A " two component vegetable mix " consisting of maize meal, two parts, and cow pea meal, one part, with added sugar. In addition, all children received a vitamin supplement, and those on the vegetable diets a mineral mixture. Balance studies were carried out (on male children only) over 3-day periods, but not in patients with severe diarrhoea or infection. Progress was also assessed clinically.

In the children given the milk diets nitrogen retention was significantly higher during the first 2 weeks than later, although nitrogen absorption was more impaired during this period than later. It is pointed out that the initial degree of protein depletion is therefore an important variable in the interpretation of nitrogen balance studies. With the diet of pure maize meal nitrogen retention was significantly less, and was not influenced by the glycine supplement; when given during convalescence this diet produced a reduction in the plasma albumin level. Supplementation of the maize with pea flour, with or without added maize germ, resulted in a significant improvement in nitrogen retention, and the supplemented diet proved capable of curing mild cases of kwashiorkor and maintaining a satisfactory concentration of serum albumin and a weight gain for as long as 150 days, at least in the conditions prevailing in the metabolic ward. It is suggested that such diets may therefore prove useful in the prevention of this disease.

[The wealth of data derived from these balance studies and presented in full in the original paper merits consideration by those interested in kwashiorkor.]

*W. H. Horner Andrews*

1424. **Diseases of Nutritional Deficiency of Children in South India: a Review of Some Salient Conditions**
C. GOPALAN. *Journal of Pediatrics* [*J. Pediat.*] **57**, 89–100, July, 1960. 34 refs.

## INFECTIOUS DISEASES

1425. **Acute Cardiac Failure in Rickettsiosis.** (L'insuffisance cardiaque aiguë au cours de rickettsioses)
P. LE GAC and P. GIROUD. *Bulletin de la Société de pathologie exotique et de ses filiales* [*Bull. Soc. Path. exot.*] 53, 20–24, Jan.–Feb. [received June], 1960. 4 figs., 9 refs.

The senior author (Le Gac) has on several occasions since 1939 reported cases of severe and sometimes fatal typhus fever occurring in savannah areas of tropical Africa during the dry season. It is particularly associated with brushwood fires, which drive rats and other rodents to seek shelter in human habitations, where they shed their parasites (fleas and ticks) and so infect the inhabitants. The disease affects both Europeans and native Africans. The authors now return to the subject because of the increasing danger, through rapid air travel, of cases of this kind occurring in persons after their return to metropolitan France.

Writing from the Institut Pasteur, Paris, they describe 6 cases, all in young adults, 3 of the patients being male Europeans, one an American woman missionary, and 2 Africans; the female patient died. As in many cases of severe typhus fever these patients all suffered from episodes of delirium, sometimes with suicidal tendencies, and in addition they all had grave attacks, either short or prolonged, of severe cardiac insufficiency. Particular stress is laid on the latter observation, and the authors link the cardiac condition with the well-known tendency of the rickettsiae to invade the vascular system. In 5 of these cases the infection was almost certainly flea-borne typhus (*Rickettsia mooseri* was isolated from 3), and one was a typical tick-borne typhus (*fièvre boutonneuse*) similar to Rocky Mountain spotted fever. Treatment is mainly supportive and may include broad-spectrum antibiotics and cardiac stimulants; convalescence is prolonged. *H. Stanley Banks*

1426. **Acute Renal Failure in Asiatic Cholera: Clinicopathologic Correlations with Acute Tubular Necrosis and Hypokalemic Nephropathy**
C. BENYAJATI, M. KEOPLUG, W. R. BEISEL, E. J. GANGAROSA, H. SPRINZ, and V. SITPRIJA. *Annals of Internal Medicine* [*Ann. intern. Med.*] **52**, 960–975, May, 1960. 2 figs., 30 refs.

From the Chulalongkorn Hospital Medical School, Bangkok, and the Walter Reed Army Institute of Research, Washington, D.C., the authors report the cases of 13 Thai patients with cholera, with necropsy reports on 5 of them, in an attempt to clarify the nature of the renal damage seen in such patients. Transient oliguria, which yields to the control of shock and replacement of fluids, is very frequent. In a few patients the disease ran the typical course associated with acute tubular necrosis and in these the oliguria persisted for many days; it was sometimes fatal, while in other cases it was followed by a diuretic phase. A rise in the plasma potassium level was exceptional, however, and this deviation from the usual findings in acute renal failure is attributed to potassium depletion caused by the profuse diarrhoea. In all of the 5 patients who died tubular necrosis was demonstrated post mortem, and 2 of these also showed the vascular degeneration of the proximal tubules which is characteristic of " kaliopenic nephropathy ". *D. A. K. Black*

1427. **Fluid and Electrolyte Disturbances in Cholera before Treatment, and the Effect of Intravenous Administration of Various Saline Solutions: a Study of Ninety-three Cases**
M. KRUATRACHUE, R. BURI, S. NA-NAKORN, V. PHANICH, C. SATHAPANAKUL, and C. TUCHINDA. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **54**, 106–111, April, 1960. 12 refs.

During an epidemic of cholera in Thailand in 1958 the authors, working at the University of Medical Sciences, Bangkok, determined the serum concentrations of sodium, potassium, and chloride ions and also the carbon dioxide combining power of the serum in 69 patients before treatment. In 33 of these patients and in another

24 who had had venoclysis before admission to hospital the effect of intravenous infusion of saline solutions on the specific gravity of the blood and on the serum electrolyte levels was assessed, measurements being made before and 30 minutes after each infusion.

Before treatment the serum sodium level was high, 30% of the patients having a concentration of over 145 mEq. per litre, while in 85% the chloride concentration was over 100 mEq. per litre; in about 66%, however, the serum potassium concentration was less than 4 mEq. per litre, presumably owing to loss of potassium in the stools. In most patients the specific gravity of the blood was 1·065 or higher. The authors conclude that in choosing solutions for intravenous therapy it is the quantity of fluid rather than its composition (isotonic, hypertonic, or hypertonic–alkaline) which is important in the initial treatment of cholera, and that isotonic saline should be used for maintenance therapy. Certain modifications of the composition of the fluid may be necessary according to the severity of the electrolyte loss. Replacement of potassium may be necessary and for this the oral route is to be preferred.

*W. H. Horner Andrews*

1428. **Clinical Evaluation Studies in Lepromatous Leprosy: a 24-Weeks' Study of Pryazinamide–Isoniazid Therapy**

J. A. DOULL, J. N. RODRIGUEZ, J. G. TOLENTINO, and J. V. FERNANDEZ. *International Journal of Leprosy* [*Int. J. Leprosy*] **28**, 12–17, Jan.–March [received July], 1960. 10 refs.

In this comparative study reported from the Philippines Department of Health, Manila, 30 patients with lepromatous leprosy were treated with pyrazinamide (30 mg. per kg. body weight) plus isoniazid (5 mg. per kg.) daily for 24 weeks; no toxic reactions occurred. A control group of 30 matched patients were treated with dapsone, beginning with 50 mg. daily and increasing to 200 mg. daily by the 10th week. After 24 weeks 6 of the patients receiving pyrazinamide plus isoniazid had improved clinically, 13 were stationary, 7 were worse, and 4 had absconded. Of the dapsone-treated patients 9 had improved, 16 were stationary, one was worse, and 4 had absconded. Bacteriologically there was no significant change for better or worse in either group. It is concluded that the results of treatment of leprosy with pyrazinamide plus isoniazid are not superior to those obtained with dapsone [in fact, the former combination might be slightly less efficacious]. *F. Hawking*

1429. **Clinical Evaluation Studies in Lepromatous Leprosy: a 48-Weeks' Study of Cycloserine Therapy**

J. A. DOULL, J. N. RODRIGUEZ, J. G. TOLENTINO, and J. V. FERNANDEZ. *International Journal of Leprosy* [*Int. J. Leprosy*] **28**, 18–21, Jan.–March [received July], 1960. 13 refs.

In this further study carried out in the Philippines [see Abstract 1428] 20 lepromatous patients were treated with cycloserine, 250 mg. daily [apparently by mouth], increased in the 3rd week to 500 mg., in the 5th week to 750 mg., and in the 7th week to 1 g. daily; treatment was continued for 48 weeks. The results were compared with those in 20 matched patients receiving dapsone in an initial dose of 50 mg. by mouth thrice weekly, increased by the 9th week to 200 mg. daily. There were no serious signs of intolerance to either drug.

Of the 14 patients given cycloserine who completed the treatment 4 showed clinical improvement, compared with 14 of the 18 completing treatment with dapsone. The " bacteriological score " for smears from skin sites fell from 25·0 to 16·2 after 48 weeks' treatment with dapsone and from 24·0 to 18·2 after that with cycloserine, while the score for smears from nasal septa declined from 7·2 to 4·2 for the dapsone group and from 7·9 to 5·7 for the cycloserine group. It is concluded that cycloserine was well tolerated, but that it showed no therapeutic superiority over dapsone [rather a slight inferiority to that drug]. *F. Hawking*

1430. **Some Recent Chemotherapeutic Work in Leprosy: with a Discussion of Some of the Problems Involved in Clinical Trials**

T. F. DAVEY. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **54**, 199–206, May, 1960. 12 figs., 7 refs.

The author, on the basis of his wide experience in leprosy control in Nigeria, describes the effects of new drugs in the treatment of leprosy and discusses the difficulties of assessing their value. Dapsone (DDS), which has become the standard treatment and provides a yardstick to measure the efficacy of any new drug, is cheap and efficient. In one area the author notes that no case of leprosy occurred during the past 9 years in the children of mothers receiving dapsone. Nevertheless there are still many drawbacks to sulphone therapy, including hypersensitive reactions and intolerance to the drug. In the assessment of a new drug it is a serious drawback that it has not yet been possible to cultivate *Mycobacterium leprae* outside the body. The author also points out that it is not certain that the organism seen in stained preparations is the same in all parts of the world.

There is much evidence to suggest that the length of time the organism has been in the body influences its susceptibility to drugs, recent infections responding more quickly to therapy than those of longer standing. It is also noted that there is no constant relationship between magnitude of the infection and size of the lesion. Recent observations suggest that the morphological appearances of the bacilli may vary with the progress of the disease. Thus fragmentation of the bacilli into a granular form is regarded as evidence that the tissue reaction is successful. Ideally new remedies should be tested on subjects who have had no previous treatment, but such patients are now becoming rather scarce. The author has been carrying out clinical trials with two recent preparations, " CIBA 1906 " and " etisul " (diethyl dithio*iso*phthalate). With Ciba 1906 the early results were good and there were no signs of toxicity and no side-effects, but unfortunately relapses were frequent after the 36th month. The author has already presented (with Hogerzeil in one paper) two progress reports on the results achieved with

etisul (*Leprosy Rev.*, 1959, **30**, 61 and 141; *Abstr. Wld Med.*, 1959, **26**, 144 and 1960, **27**, 20). This drug has an objectionable odour which, however, can be disguised to some extent by adding a perfume. He considers that both these drugs have a place in the treatment of leprosy. *William Hughes*

**1431. A Combination of Amodiaquin and Primaquine (Camoprim) in the Prevention and Cure of Sporozoite-induced Chesson Strain *Vivax* Malaria**

K. O. COURTNEY, R. HODGKINSON, R. RAMSEY, and M. HAGGERTY. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **9**, 149–154, March, 1960. 2 figs., 15 refs.

An investigation was undertaken at the State Prison, Raiford, Florida, to assess the possibility of using a mixture of amodiaquine and primaquine for mass chemotherapy in malarious areas where, for one reason or another, residual insecticides could not be employed. A total of 18 white prisoners volunteered to take part and each was bitten and rebitten by *Anopheles quadrimaculatus* infected with the Chesson strain of *Plasmodium vivax* until 10 positive bites had been received.

In the first part of the trial 6 subjects received 300 mg. of amodiaquine base and 30 mg. of primaquine base (" one dose ") weekly for 8 weeks before infection and for 10 weeks afterwards. None developed fever and no parasites could be found in the blood during a period of over 6 months. Clean mosquitoes fed on the subjects 20, 22, and 24 days after they had been bitten failed to become infective.

In the second part, all the 9 volunteers who remained in the trial received a single dose of 600 mg. of amodiaquine base 20 days after infection. This treatment was rapidly effective; chills and fever stopped within one day and parasites disappeared from the blood stream within 24 to 36 hours. Subsequent doses of " camoprim ", a combination of amodiaquine and primaquine, weekly in 5 volunteers and fortnightly in 4, to a total of 10 doses, resulted in radical cure in all cases. Mosquitoes fed on the volunteers 36 and 72 hours after the single dose of amodiaquine failed to become infective.

*I. M. Rollo*

**1432. Effect of Malaria Control on Haemoglobin Levels**

C. C. DRAPER. *British Medical Journal* [*Brit. med. J.*] **1**, 1480–1483, May 14, 1960. 1 fig., 15 refs.

In the study of the effect of malaria control on the health of the population, as estimated by haemoglobin levels, here reported from the East African Institute of Malaria, African dwellings in an experimental area of the Taveta and Pare districts of Kenya and Tanganyika were sprayed annually with the residual insecticide dieldrin 6 times between 1954 and 1959. A considerable reduction in the transmission of malaria occurred, parasite rates decreasing more than 10-fold and spleen rates being reduced in all age groups. More than 90% of the infections were due to *Plasmodium falciparum*. Haemoglobin levels were determined on 5 occasions on some 2,000 people in the experimental (sprayed) area, similar control surveys being carried out in smaller groups of people in a lowland area 70 miles away in which malaria was uncontrolled, and also at a school in a malaria-free area in the Pare mountains. Schistosomiasis and hookworm infection were common in the sprayed area throughout the experiment.

During the period of malaria control there was a progressive rise in the mean haemoglobin values in all age groups, the greatest proportional increases being noted in the non-immune infants and young children and the least in girls and young adult females; there was also a small rise in the mean total leucocyte counts. Analysis of the data showed that low haemoglobin levels were correlated with splenomegaly. Haemoglobin levels in the area in which malaria was not controlled remained unchanged during the period of the experiment. At the school in the malaria-free district, a small increase in haemoglobin values was observed, which the author considers may have resulted from development of the area and consequent improved living conditions. It is concluded that the rise in haemoglobin levels was probably due to the reduction of malaria transmission, but that a general rise in living standards which took place during the observation may also have had some effect.

*L. G. Goodwin*

**1433. Sickling and Malaria in South-west Nigeria**

J. P. GARLICK. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **54**, 146–154, March [received June], 1960. 2 figs., 18 refs.

Two series of children from out-patient clinics in Ibadan, W. Nigeria, showed reduced *Plasmodium falciparum* rates and densities in sicklers. In a series of older school-children no reduction in rate and little lowering of the mean density was found. Children complaining of fever showed a conspicuously lower sickling rate than a control group. The *P. malariae* parasite rate for sicklers was reduced in all series. The distribution of sickling between mothers and children suggests the possibility of a relatively greater number of successful pregnancies for sickler women.—[Author's summary.]

**1434. Diloxanide (" Entamide ") in the Treatment of Amoebiasis**

S. P. MEHTA, F. T. PADARIA, and M. M. RATHI. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **63**, 93–95, April, 1960. 1 ref.

A clinical trial of diloxamide (" entamide "), an anilide derivative, in the treatment of amoebiasis is reported from Grant Hospital, Bombay. The drug was given in doses of 20 mg. per kg. body weight daily for 10 days to 24 patients whose stools were positive for *Entamoeba histolytica*, 2 of whom had hepatic complications. Though well tolerated, the drug rendered the stools cyst-free in only 17 of these cases, and in only 9 of these did the stools remain cyst-free after another 14 days. It had no effect in hepatic amoebiasis. It is concluded nevertheless that the drug deserves further trial.

[The manufacturers of entamide are producing other variations of the formula which may be more effective.]

*Clement C. Chesterman*

# Allergy

**1435. Prolonged Corticosteroid Therapy in Chronic Asthma**

A. R. Somner, M. C. Rogan, and I. W. B. Grant. *British Medical Journal* [*Brit. med. J.*] **1**, 1092–1097, April 9, 1960. 3 figs., 8 refs.

The treatment of chronic asthma has been the subject of considerable, and at times fierce, controversy. In this study, carried out at the Northern General Hospital, Edinburgh, the authors have compared the effect of intermittent steroid therapy with that of continuous long-term treatment in the hope that in this way the side-effects so liable to result from long-term steroid therapy might be avoided. In the 33 cases of chronic asthma studied the symptoms had been severe and relatively constant for at least 2 years and had failed to respond to bronchodilator drugs; many of the patients had chronic bronchitis in addition to asthma.

All patients were initially given a preliminary course of cortisone (100 to 200 mg. daily) or prednisolone (20 to 40 mg. daily) for at least 7 days before long-term therapy was begun. Thereafter 20 adult patients with asthma of moderate severity were divided into two groups and given intermittent treatment, 10 (Group A) receiving 5 mg. of prednisolone 4 times daily on 2 consecutive days per week, and the other 10, matched for age and sex (Group B), being given the same daily dose for the first 8 days of each 4-week period; thus both groups received a total of 160 mg. in each 4-week period, this being maintained for 20 weeks in 19 cases and for 16 weeks in one. A clinical assessment together with measurement of the forced expiratory volume (F.E.V.) was made every 4 weeks on the day before resumption of treatment. During the second phase of treatment, which lasted for 12 weeks, the dose of prednisolone given was increased by 50% by giving 20 mg. daily for 3 days at the beginning of each week to Group A and for 6 consecutive days each fortnight to Group B; 12 patients entered this second phase of the trial, 5 from Group A and 7 from Group B. A third group (Group C) consisting of 14 patients with more severe chronic asthma were treated continuously with prednisolone, 5 mg. 3 times a day (or twice daily in the case of children under 14 years of age) for 15 months. In 9 cases triamcinolone in a dosage of 6 to 12 mg. daily was later substituted.

In Groups A and B at the end of Phase 1 of intermittent treatment the results of 50 clinical assessments were as follows: Group A, 23 satisfactory, 20 fair, and 7 unsatisfactory, while for Group B the corresponding figures were 22, 18, and 10. In both groups the mean value of $F.E.V._1$ was increased above the pre-treatment level on each occasion. In the last 4 to 8 weeks, however, this value was well below the level recorded after the initial 7 days of intensive treatment. During Phase 2 the number of assessments classified as satisfactory rose to 25 in Group A and to 36 in Group B. At some time in the trial, but not before the completion of 16 weeks' therapy, prednisolone was replaced by inert tablets in 18 patients in Groups A and B without the knowledge of the patient or the supervising physician. As a result marked deterioration was observed within 4 weeks in 9 cases, moderate deterioration in 3, and slight deterioration in 4. In several cases the deterioration was so severe as to require emergency hospital treatment. Of the 14 patients in Group C given continuous steroid therapy 8 responded dramatically, and eventually became asymptomatic, 3 improved to a moderate extent, and 3 failed to respond. The well-known side-effects such as moon-face and excessive weight gain were observed in all patients given continuous therapy but in none of those receiving intermittent therapy; of the 9 patients who were changed to triamcinolone 5 showed some loss of weight. In addition 4 patients in Group C developed serious side-effects, osteoporosis and fracture occurring in 2 patients, tuberculosis in one, a girl aged 10, and peptic ulcer in a woman aged 54. Evidence of severe adrenal depression, with failure to respond to corticotrophin stimulation, has been found in all but 2 of the 11 patients receiving prednisolone or triamcinolone therapy continuously for over 1 year.

The authors conclude that continuous therapy is more effective than intermittent therapy, but more serious side-effects must be expected. Chronic bronchitis adversely affects the results of prednisolone therapy.

[These results are in keeping with the experience of other workers, since both the degree of improvement and the severity of side-effects are related to the dosage of steroid administered. The incidence of serious side-effects in this study is rather higher than that reported by other workers and clearly implies that continuous steroid therapy should be undertaken only in really severe cases of asthma.] *R. S. Bruce Pearson*

**1436. Evidence of Allergy in Patients with Cystic Fibrosis of the Pancreas**

T. E. Van Metre Jr., R. E. Cooke, L. E. Gibson, and W. L. Winkenwerder. *Journal of Allergy* [*J. Allergy*] **31**, 141–150, March–April, 1960. 1 fig., 8 refs.

During the past 3 years the authors have observed 6 patients at the Johns Hopkins Hospital, Baltimore, with both allergic asthma and cystic fibrosis of the pancreas. Of 135 patients with cystic fibrosis seen at the same hospital since 1939, 19 could be shown also to have suffered from some form of atopic allergy. In 47 consecutive patients with allergic asthma seen by the authors cystic fibrosis could be excluded as there was no increase in the chloride concentration of the sweat. The association of allergy and cystic fibrosis may be the chance coincidence of 2 unrelated disorders, but the possibility is discussed that cystic fibrosis supports the development of allergy or alternatively that allergy favours survival in cystic fibrosis. *H. Herxheimer*

# Nutrition and Metabolism

1437. **Serum Vitamin $B_{12}$ Concentration in Dietary Deficiency**

J. A. HALSTED, J. CARROLL, A. DEHGHANI, M. LOGHMANI, and A. S. PRASAD. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **8**, 374–376, May–June, 1960. 1 fig., 4 refs.

At the Veterans Administration Hospital, Syracuse, New York, the serum vitamin $B_{12}$ (cyanocobalamin) concentration was determined in the blood of 23 Iranian villagers living on a diet almost devoid of animal protein and in that of a further 23 whose diet was fairly rich in vitamin $B_{12}$. All the subjects were hospital patients not suffering from disease known to affect the metabolism of this vitamin. The analyses were performed in Syracuse 8 days after the blood samples had been withdrawn in Iran, during which time they were kept frozen; it had been previously shown that the vitamin $B_{12}$ content of serum is not changed after 10 days in the frozen state.

The mean serum vitamin $B_{12}$ level in the group taking the low-protein diet was 411 $\mu\mu$g. per ml. (range 117 to 960 $\mu\mu$g. per ml.) and in the other group 518 (range 133 to 1,300) $\mu\mu$g. per ml. As these figures show, the scatter of the findings was wide in both groups and the difference in means between the groups was not statistically significant, nor did the values found differ significantly from those obtained in 333 healthy subjects in Syracuse. It is concluded from this study that vitamin-$B_{12}$ deficiency resulting solely from a diet poor in animal protein must be rare. *H. E. Magee*

1438. **The Syndrome of Magnesium Deficiency in Man**

S. HANNA, M. HARRISON, I. MACINTYRE, and R. FRASER. *Lancet* [*Lancet*] **2**, 172–176, July 23, 1960. 2 figs., 21 refs.

From the Postgraduate Medical School of London the authors report 3 cases of pure magnesium deficiency in man, with a resumé of all the essential metabolic data. They are at pains to emphasize that tetany is not an essential feature of magnesium deficiency. They admit that Chvostek's sign is usually positive, but are careful to report the absence of Trousseau's sign even after 8 minutes' compression and the absence of spontaneous muscle cramps in their cases. They suggest that the tremors, choreiform movements, fibrillary twitches, athetoid movements, and convulsions frequently described in association with magnesium deficiency in man have tended erroneously to be attributed to tetany.

After a careful analysis of the data from previously reported cases the authors conclude that the tetany observed occurred only when the magnesium deficiency was associated with a low serum calcium level, which they do not consider to be a necessary concomitant of the syndrome, since hypomagnesaemia may occur without evidence of other electrolyte deficiencies. The essential features of the syndrome of magnesium deficiency in man, all of which rapidly disappear on restoration of the serum magnesium level to normal are considered to be: (1) a positive Chvostek's sign with a negative Trousseau's sign; (2) a low-voltage electrocardiogram; (3) liability to epileptiform convulsions; and (4) depression, vertigo, ataxia, and muscular weakness. *R. E. Tunbridge*

1439. **Phenmetrazine Hydrochloride and Methylcellulose in the Treatment of " Refractory " Obesity**

L. J. P. DUNCAN, K. ROSE, and A. P. MEIKLEJOHN. *Lancet* [*Lancet*] **1**, 1262–1265, June 11, 1960. 7 refs.

Phenmetrazine hydrochloride (" preludin ") is said to possess the appetite-reducing power of the amphetamines without their undesirable attributes. Methylcellulose is an inert, indigestible substance which swells up in the stomach and small intestine and may thus produce a sense of repletion. In a double-blind controlled trial carried out at the Royal Infirmary, Edinburgh, these drugs were given to 85 obese out-patients who had failed to lose weight in the past 3 months despite the prescription of reducing diets providing 1,100 to 1,600 Calories daily. For the purpose of the trial each patient was instructed to adhere to the diet previously prescribed and to attend for observation once a fortnight.

The trial was divided into 3 consecutive periods, and the patients were divided into 3 groups (A, B, and C). During the first period (4 weeks) all groups received dummy tablets; the results for this period showed that only a few patients lost weight. During the second period (8 weeks) Group A continued to take dummy tablets, Group B took 0·5 g. of methylcellulose 3 times daily, and Group C took 25 mg. of phenmetrazine twice daily; Groups A and B showed little change in weight, but there was a highly significant loss of weight in Group C, a mean of 6·0 lb. (2·72 kg.) being lost during the period. It was clear, therefore, that methylcellulose was having little effect and this substance was dropped from the trial. During the third period (8 weeks) Groups A and B took phenmetrazine in the increased dose of 25 mg. 3 times daily, while Group C received dummy tablets; the first two groups now showed mean losses of 4·1 lb. (1·86 kg.) and 2·8 lb. (1·27 kg.) respectively, whereas Group C now showed a mean gain of 2·0 lb. (0·91 kg.).

It is pointed out that the loss of weight produced by phenmetrazine, though statistically significant, was disappointingly small. No important side-effects resulted from its use in a dose of 50 mg. daily, but with 75 mg. daily 5 patients complained of insomnia and 2 of a return of angina pectoris. Only 5 of the 85 patients admitted that they had less desire for food when taking phenmetrazine. However, 7 patients have since asked for a renewed supply of the drug, " which raises the serious question of addiction ". Because of this danger, the high cost of the drug, and its small effect on appetite the authors " do not regard phenmetrazine as a good drug for the routine treatment of obese patients ". *Joseph Parness*

# Gastroenterology

1440. **Local Corticosteroid Treatment in Severe Attacks of Ulcerative Colitis**
S. C. TRUELOVE. *British Medical Journal* [*Brit. med. J.*] 2, 102–108, July 9, 1960. 1 fig., 16 refs.

In this further paper from the Radcliffe Infirmary, Oxford, the author assesses the role of steroids in the treatment of severe cases of ulcerative colitis. Although these drugs are not so effective as in milder cases, it is clear that they play a vital role in the management of many cases, as is demonstrated by the 5 case reports presented in some detail. The regimen recommended is summarized as follows: correction of dehydration and electrolyte depletion; blood transfusions to maintain the haemoglobin value at a high level; a high caloric intake with added vitamins; the systemic administration of a steroid, usually prednisolone, and local administration, preferably of hydrocortisone hemisuccinate, twice daily by rectal drip, together with intravenous propantheline to reduce intestinal motility.

The author considers that the reduction in the case-fatality rate from ulcerative colitis in two Oxford hospitals since 1956 is largely if not entirely due to the use of local steroid therapy. *A. Gordon Beckett*

1441. **Changes in the Skin and Its Appendages in Patients Subjected to Gastric Resection.** (К изменениям кожи и ее придатков у больных, подвергшихся резекции желудка)
V. MEL'CER and M. MEL'CER. *Вестник Дерматологии и Венерологии* [*Vestn. Derm. Vener.*] **34**, 18–21, July, 1960. 13 refs.

The authors report that trophic disorders of the skin and the hair are often observed in patients who have undergone gastric resection. These changes consist of pallor, dryness, desquamation and haemorrhagic tendencies. The hair tends to fall out, and what is left often becomes light in colour and brittle. In men, growth of the beard is retarded. There is also increased sensitivity to sunlight. These changes are considered to be due to a decrease in the serum protein content and to avitaminosis. Other reports in the literature describing this condition are briefly reviewed. *N. Hopewell*

1442. **Esophageal Acid Perfusion Test and a Gastro-esophageal Reflux Test in Patients with Esophagitis**
S. G. TUTTLE, A. BETTARELLO, and M. I. GROSSMAN. *Gastroenterology* [*Gastroenterology*] **38**, 861–872, June, 1960. 5 figs., 25 refs.

In an attempt to increase the accuracy of diagnosis of oesophagitis the authors, working at Wadsworth Veterans Administration Hospital and the University of California Medical Center, Los Angeles, have used two new procedures in the investigation of 124 patients, including 7 with gastric ulcer, 61 with duodenal ulcer, and 26 with hiatal hernia. There were 118 men and 6 women, with an average age of 50·2 (range 24 to 84) years. In the first test a nasogastric tube was passed into the stomach, the gastric contents were aspirated, and the tube was then withdrawn into the oesophagus until its lower end was 25 cm. from the nares. Decinormal hydrochloric acid was then perfused into the oesophagus at the rate of 10 ml. per minute for 30 to 60 minutes or until " definite symptoms " appeared, when the acid was replaced by normal saline. [It is not clear what happened to the perfusing fluid, but as there is no mention of a double-lumen tube it was presumably allowed to pass into the stomach.] A positive response consisted in the duplication of the patient's spontaneous symptoms when the acid was administered and their rapid relief when saline was substituted. The importance of the rapidity of this relief is emphasized—in the presence of a peptic ulcer pain might be caused by acid passing into the stomach; such pain, however, is said never to be relieved rapidly on changing over to saline. The second test consisted in recording simultaneous measurements of *p*H and pressure at various levels in the oesophagus, acid reflux being diagnosed " when a *p*H of 4 or less was encountered over an area extending at least 4 cm. above the pressure inversion point ", that is, the level at which the positive inspiratory pressure in the abdomen is replaced by the negative inspiratory pressure in the chest.

Excellent correlation was obtained between the clinical, radiological, and endoscopic findings and the results of the two tests. [The figures are not clearly tabulated.] Of the 43 patients with no symptoms of oesophagitis, none gave a positive response to the acid perfusion test and only 3 to the reflux test; of these 3, 2 had oesophageal varices. Of the 81 patients with symptoms, 79 gave evidence of reflux and 66 a positive response to the perfusion test. The absence of a positive response in some cases was ascribed to treatment with antacids, which seems slowly to desensitize the oesophagus even though reflux continues. In 2 patients with extensive strictures there had been no symptoms for a long time and there was no response to acid; it was assumed that the oesophagus had become insensitive. *Denys Jennings*

1443. **X-ray and Clinical Features of Hiatal Hernia: Significance of Hiatal Hernias of Minimal Degree**
H. J. TUMEN, G. N. STEIN, and E. SHLANSKY. *Gastroenterology* [*Gastroenterology*] **38**, 873–883, June, 1960. 4 figs., 13 refs.

The incidence of hiatal hernia as recorded by different radiologists varies from 1 or 2% to as high as 70%. By the methods of barium-meal examination and film interpretation which is recommended in this paper from the Graduate Hospital of the University of Pennsylvania, Philadelphia, a hiatal hernia may be diagnosed in 50% of all adults.

To determine the significance of hiatal hernias of minimal degree the authors examined the radiographs of 300 consecutive patients undergoing barium-meal examina-

tion. In 169 of these cases, in which adequate films of the oesophago-gastric junction were available, the clinical history was studied and an attempt was made to correlate the clinical features with the x-ray findings. Hiatal hernias were diagnosed radiologically in 113 cases, being classified in three grades. In a Grade-I hernia only the gastro-oesophageal vestibule, that is, the part below the inferior oesophageal sphincter, appeared above the diaphragm; Grade-II hernias contained a small knuckle of stomach 2 to 3 cm. in diameter; and Grade III consisted of the larger hernias. [All the hernias found were apparently of the sliding type. There is no mention of para-oesophageal or mixed types.] The following table shows the relation of these findings to the clinical findings.

| X-rays Findings | Clinical Evidence of Hernia | | | |
|---|---|---|---|---|
| | Negative | Questionable | Positive | Total |
| Negative.. .. | 34 | 11 | 11 | 56 |
| Grade I .. .. | 32 | 9 | 45 | 86 |
| Grade II.. .. | 6 | 2 | 13 | 21 } 113 |
| Grade III .. | 0 | 2 | 4 | 6 |
| Total .. | 72 | 24 | 73 | 169 |

The loose correlation found between symptoms and x-ray findings was considered to support the authors' view that hiatal hernia was not being over-diagnosed radiologically. It is pointed out that in 11 cases in which a definite clinical diagnosis of hiatal hernia was made the x-ray findings were negative, possibly suggesting that with better or repeated radiology the frequency of diagnosis would be even higher. The radiological diagnosis of hernia in 38 patients with no symptoms " emphasizes the well known fact that hernias may be present without producing symptoms ". No relation could be found between the size of the hernia and the severity of the symptoms, and it is tentatively concluded that the latter are probably entirely the result of the reflux of acid into the oesophagus. [The view that repeated reflux is the cause of hiatal hernia, and not the result, is not mentioned.] *Denys Jennings*

## LIVER DISEASES

### 1444. The Use of Vasopressin (" Pitressin ") in the Control of Bleeding from Oesophageal Varices

S. SHALDON and S. SHERLOCK. *Lancet* [*Lancet*] **2**, 222–225, July 30, 1960. 1 fig., 19 refs.

The authors describe the use of vasopressin in the treatment of 8 patients with hepatic cirrhosis and portal hypertension who were treated at the Royal Free Hospital, London, all of whom had bled from oesophageal varices for 6 to 72 hours (average 16 hours) before the administration of vasopressin, it having proved impossible to control the bleeding by blood transfusions. None of the patients was considered fit for emergency surgery and all had some degree of liver failure. In 5 cases the portal pressure was measured by percutaneous splenic puncture and in 2 by the wedged hepatic-venous method.

Treatment for impending hepatic coma was first given, including intravenous hypertonic glucose, attention to electrolyte balance, and administration of neomycin (in a dosage of 4 g. daily by mouth). Then after a preliminary electrocardiogram had been taken, since vasopressin is said to constrict the coronary arteries, 20 units of this substance in 1 ml. diluted with 100 ml. of 5% dextrose was given intravenously over a 10-minute period. The stomach was aspirated every 30 minutes, control of the bleeding being estimated by disappearance of blood from the gastric juice and by the results of serial blood pressure and pulse recordings. In all 8 patients haemorrhage ceased within one hour of administration of vasopressin. In 3 it did not recur, and the condition of 2 became such as to permit the performance of portacaval anastomosis. In a 4th patient there was only one further haemorrhage, after 36 hours, but the patient died 8 days later in coma. In the remaining 4 patients vasopressin was successful initially in controlling the bleeding, but this recurred later and although the drug was given repeatedly at 4-hourly intervals all 4 patients died within 5 days with a massive terminal haemorrhage.

In 7 patients portal hypertension (mean 26 mm. Hg) was present during the bleeding, while the systemic blood pressure was not markedly reduced. After vasopressin the portal venous pressure fell to a mean of 14 mm. Hg; in one patient serial determinations showed a return to base level within 60 minutes. No adverse side-effects were noted with vasopressin, and its use is suggested as an alternative to the Sengstaken oesophageal compression tube, which has many disadvantages and is extremely unpleasant for the patient. *W. H. Horner Andrews*

### 1445. Ammonia Tolerance in Liver Disease

H. O. CONN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **55**, 855–871, June, 1960. 4 figs., 49 refs.

At Yale University and the West Haven Veterans Administration Hospital, New Haven, Connecticut, the author has investigated the " ammonia tolerance " in a group of subjects with and without liver disease by measuring the venous blood ammonia levels in the fasting state and again 45 and 120 minutes after the oral administration of 3 g. of ammonium chloride. Assessment of hepatic function by means of standard liver function tests and by needle biopsy of the liver together with oesophagoscopy for the detection of oesophageal varices were also carried out.

In 18 normal subjects and 7 patients with non-hepatic disorders the mean fasting venous ammonia level was 102 (range 60 to 150) $\mu$g. per 100 ml. and after administration of ammonium chloride there was no significant change. In 18 out of 19 patients with obstructive jaundice the ammonia tolerance test result was also normal while of 22 patients with viral or drug induced hepatitis all but 6 showed normal results. Of these latter 2, or possibly 3, had oesophageal varices. However, of 60 patients with hepatic cirrhosis, of whom about half showed clinical evidence of liver cell failure the ammonia tolerance test was abnormal in 50, there being an abnormally high fasting value and a high and sustained rise in venous

ammonia levels following ammonium chloride. In 18 patients with cirrhosis and a portacaval shunt the fasting venous ammonia level was elevated and the rise following ammonium chloride was higher than in the group with cirrhosis alone.

The author concludes that in hepatitis ammonia tolerance may be normal, but this is likely to be related to the presence of portal–systemic anastomoses—as evidenced by the presence of oesophageal varices—rather than to be due to poor liver cell function. Severe hepatocellular failure may co-exist with normal ammonia tolerance; in cirrhotic patients there was a better correlation between abnormal ammonia tolerance and the presence of portal hypertension rather than with the degree of liver cell failure. Of 10 cirrhotic patients in whom the ammonia tolerance test was normal the cirrhosis in 6 was mild with no portal hypertension; the normal result of the test in the other 4 patients who had both liver cell failure and portal hypertension was more difficult to explain. It may be that the peripheral tissues in such patients extract more ammonia from the blood, with a consequent lowering of the venous ammonia level. The arterial level in such cases may be more representative of the true state of affairs and was shown to be elevated in one of the patients with normal venous ammonia levels. The fact that the patients with a portacaval shunt showed the greatest abnormality in ammonia tolerance, despite the fact that their liver-cell function was less deranged than that of the cirrhotic patients, is also in favour of the concept of abnormal ammonia tolerance being a reflection of the presence of portal–systemic anastomoses.

In conclusion the author suggests that the ammonia tolerance test, performed as he describes, is a reliable method for detecting the presence of a portal–systemic collateral circulation. *A. E. Read*

1446. **Ammonium Tolerance Test: a Diagnostic Aid in Liver Diseases.** [In English]
J. EGENSE. *Acta medica Scandinavica* [*Acta med. scand.*] **167**, 53–59, 1960. 5 figs., 14 refs.

The author has studied at Bispebjerg Hospital, Copenhagen, the " ammonia tolerance " of patients with and without liver disease. Blood samples from a peripheral artery and antecubital vein were taken in the fasting state and the ammonia level determined by the Seligson technique. After 10 g. of ammonium citrate had been given by mouth further samples of venous blood were withdrawn at 30, 60, 120, and 180 minutes.

Four groups were studied, with the following results. (1) In 4 normal subjects the blood ammonia concentration was unchanged after ingestion of ammonium citrate; (2) of 8 patients with doubtful liver disease 3 patients gave a normal test result, 3 others had high fasting blood ammonia levels, and 2 showed completely abnormal ammonia tolerance, with high fasting ammonia levels initially and a further rise after ammonium citrate; (3) in 5 patients with cirrhosis the fasting blood ammonia value was normal (0·46 to 1·34 $\mu$g. per ml.), but all showed abnormally high levels in the venous blood samples after loading; (4) lastly in 6 patients with cirrhosis and a collateral circulation, as shown by the presence of oesophageal varices, or with a surgically constructed portacaval shunt, both fasting and subsequent blood ammonia levels were abnormal. The rise in ammonia level was greatest in this group.

The author considers that an abnormal result of the ammonia tolerance test points to the diagnosis of hepatic cirrhosis. Although the numbers were admittedly small, no patient with severe cirrhosis showed normal ammonia tolerance. It is possible that some patients with apparently normal ammonia tolerance would show an abnormal response if arterial ammonia values were measured, since ammonia can be removed by muscle tissue and the venous blood level therefore reduced. Of 3 patients in whom both arterial and venous blood ammonia levels were determined one showed a normal venous blood level but an abnormal arterial blood level. A similar study in one other patient with chronic hepatic pre-coma revealed a marked difference between arterial and venous blood ammonia levels, which the author suggests could represent peripheral adaptation and removal of ammonia by the muscles. It is concluded that this test of ammonia tolerance is not without risk of producing neuropsychiatric deterioration in patients with liver disease, and is most informative when both arterial and venous blood ammonia levels are estimated. *A. E. Read*

1447. **Transaminases in Hepatic Tissue and Serum in Hepatic Disease**
R. L. SOMMERVILLE, G. A. FLEISHER, W. H. DEARING, G. A. HALLENBECK, and M. B. DOCKERTY. *Gastroenterology* [*Gastroenterology*] **38**, 926–936, June, 1960. 2 figs., 7 refs.

A study of the transaminase activity in hepatic tissue and serum in various liver diseases is reported from the Mayo Clinic. The enzymes studied were glutamic oxalacetic transaminase (G.O.T.) and glutamic pyruvic transaminase (G.P.T.), and their activity was determined in wedge biopsy specimens of hepatic tissue obtained at operation from 9 patients with cirrhosis (7 with Laennec's cirrhosis and 2 with post-hepatitic cirrhosis), 11 patients with obstructive jaundice, and 23 control subjects without evidence of hepatic disease.

In the liver the highest mean level of G.O.T. activity and the lowest mean level of G.P.T. activity were found in the group with cirrhosis. " A direct correlation was not evident between transaminase activities in the liver and the corresponding preoperative activities in the serum." However, the G.O.T. activity in the liver expressed as a quotient of G.P.T. activity was significantly higher in the cirrhotic group than in the others, while the serum G.O.T. activity similarly expressed was usually higher in the cirrhotic than in the control group. The transaminase activity in the serum had usually increased by the end of operation and reached a maximum one to 2 days later. Thereafter G.P.T. activity declined more slowly than G.O.T. activity.

It is suggested that the serum transaminases both before and after operation originate for the most part from the liver. *E. Forrai*

# Cardiovascular System

1448. **The Resorptive Capacity of the Skin Capillaries in Hypertensive Disease and in Myocardial Infarction.** (О резорбционной способности кровеносных капилляров кожи при гипертонической болезни и инфаркте миокарда)

O. V. KRUTOVSKAJA. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **38**, 90–94, June, 1960. 1 fig., 10 refs.

In an attempt to elucidate the nature of the changes in the resorptive capacity of the skin capillaries in various stages of hypertensive disease and in myocardial infarction and to assess their prognostic and practical significance an intradermal fluorescein test was carried out on 125 patients with hypertension, 28 patients with myocardial infarction, and 31 healthy control subjects. An injection of 0·2 ml. of a 1:50,000 solution of fluorescein was given into the skin on the inner aspect of the forearm. The fluorescence of the resulting papule was then observed by long-wave ultraviolet light and the time interval from injection to disappearance of fluorescence was noted.

In the controls this resorption time ranged from 90 to 120 minutes. It was reduced in 6 of the 14 patients with hypertensive disease in Stage I, in 34 of the 63 in Stage II, and in 26 of the 48 in Stage III. There was a direct relationship between the clinical condition of patients in Stage III and the resorption time, which was reduced to between 30 and 40 minutes in all patients with circulatory failure. The resorption time was reduced to 60 to 70 minutes in all fatal cases of myocardial infarction. In 5 cases the test was carried out during anginal attack, when the resorption time was reduced to 50 minutes. In 4 of 16 patients with myocardial infarction who survived, the resorption time was not diminished (86 to 100 minutes), and in the remaining 12 it ranged from 66 to 80 minutes.

A reduction in the fluorescein resorption time in myocardial infarction and in Stage-III hypertensive disease can thus serve as an index of incipient circulatory failure. No clear relationship could be established between the resorption time on the one hand and the morphological picture of the blood, the blood pressure, or the prothrombin index on the other. *S. W. Waydenfeld*

1449. **Pulmonary Stenosis with Intact Ventricular Septum and Fallot's Tetralogy: Assessment of Postoperative Results by Auscultation and Phonocardiography**

L. VOGELPOEL and V. SCHRIRE. *American Heart Journal* [*Amer. Heart J.*] **59**, 645–666, May, 1960. 11 figs., 22 refs.

A study has been made [at Groote Schuur Hospital, Cape Town] to determine the value of auscultation and phonocardiography in assessing the result of surgery in cases of pulmonary stenosis with intact ventricular septum and Fallot's tetralogy.

In cases of pulmonary or infundibular stenosis with an intact ventricular septum, a successful valvotomy or infundibular resection resulted in marked shortening and softening of the murmur and reduction in the width of splitting of the second sound. Less adequate relief of stenosis caused less shortening of the murmur and less reduction in the splitting.

In cases of Fallot's tetralogy, a successful valvotomy or infundibular resection (Brock operation) resulted in marked lengthening and intensification of the murmur and, frequently, the emergence of a very soft, audible pulmonary second sound widely separated (average 0·09 second) from the aortic second sound. These changes reflected increased volume rate of pulmonary flow through the stenosis and a rise in pulmonary arterial pressure. Less adequate relief of stenosis caused less prolongation of the murmur and no emergence of a pulmonary second sound. Criteria are given for grading the postoperative result.

Auscultation was shown to be an excellent bedside method of predicting the surgical result of a valvotomy in the two conditions, since the change in the length of the murmur and the width of splitting developed rapidly, and accurately reflected the degree to which the stenosis had been relieved. The opposite behavior of the murmur was due to the different dynamic situation in the two conditions. The observations proved that the length of the murmur was directly related to the severity of the stenosis when the ventricular septum was intact, but inversely related in cases of the tetralogy.

Following complete valvotomy under direct vision, the right ventricular pressure may fail to drop adequately because of severe subvalvular muscular hypertrophy. The resultant secondary infundibular stenosis may or may not regress over a period of time. The value of serial sound tracings in detecting the trend is emphasized. Gradual shortening of the initially prolonged murmur and narrowing of the split second sound indicate gradual reduction of right ventricular pressure and stenosis.

A successful Blalock–Taussig operation for the tetralogy did not lengthen the pulmonary systolic murmur, since the stenosis was not relieved by this operation. This indirectly confirmed the view that the length of the murmur is a function of the degree of stenosis, provided that the systemic resistance remains constant. However, auscultation was of value in other respects. The development of a loud continuous murmur, especially if associated with the emergence of a recordable pulmonary second sound, ensured a good result from this operation.

The use of auscultation in evaluating the result of the operation for complete repair of the septal defect and relief of the stenosis in cases of the tetralogy is discussed. The ideal end result is either a short ejection systolic murmur and narrow splitting of the second sound or no murmur at all, with normal heart sounds. The use of amyl-nitrite inhalation and phenylephrine in determining the origin of a residual systolic murmur is discussed.—[From the authors' summary.]

1450. **The Surgery of Atrial Defects with Special Reference to the Septum Primum**
R. NICKS and A. F. GRANT. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 201–206, Aug. 6, 1960. 1 fig., 3 refs.

## MYOCARDIUM

1451. **Electrocardiographic Findings after Work in Patients with Various Types of Myocardial Disease.** (Электрокардиографические изменения после работы у лиц с различными заболеваниями миокарда)
F. I. KARAMYŠEV. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **38**, 29–36, June, 1960. 3 figs.

To determine the effect of an ordinary day's work in a factory on the condition of the myocardium the electrocardiogram (ECG) and blood pressure were recorded, clinical examination of the heart and respiratory system carried out, and the prothrombin coefficient and viscosity of the blood determined before and after work in a group of 105 employees of a Moscow factory suffering from various types of heart disease. The group consisted of 34 cases of atherosclerotic heart disease (21 with coronary insufficiency), 54 cases of hypertensive heart disease (25 with coronary insufficiency), and 17 cases of myocarditis associated with valvular disease (9 with coronary insufficiency). Of these, 75 individuals were classified as capable of work. During the period of observation (1952–57) 5 patients left work and 11 died.

In 30 cases the patient remained subjectively well throughout the day and ECGs taken before and after work were identical. In 57 cases the ECG after work showed changes which could be interpreted as evidence of improvement in the condition of the myocardium as a result of work—for example, a negative T wave becoming isoelectric or even positive, a displaced S–T interval returning to the isoelectric line, and systole becoming shortened and diastole extended. In 18 cases the ECG after work showed unfavourable changes; 10 of these patients felt reasonably well, 6 completely well, and 2 unwell. There were no significant differences in the prothrombin coefficient and blood viscosity before and after work. The blood pressure increased in 52 cases, remained unaltered in 16, and diminished in 37.

From the analysis of his findings the author concludes that deterioration in the ECG after a day's work is most likely to occur when the initial tracing shows marked changes. On the other hand in the presence of increased blood pressure the ECG is labile and the tendency to favourable changes during work is more marked. The more accentuated the evidence of coronary insufficiency, the more frequently will ECG changes be found, while work associated with much neuropsychological effort more frequently has an unfavourable effect on the ECG than work involving purely physical effort. In patients with marked changes in the ECG the blood pressure tends to be labile and a rise after work is common. Among patients with atherosclerosis or hypertension the blood pressure rises more often in those with than in those without coronary insufficiency. A rise in blood pressure is also more likely to occur after work involving much neuropsychological effort than after purely physical work.

In general it would appear that, under conditions of careful resettlement, work involving no more than moderate mental and little physical effort has a favourable influence on the patient's condition and produces no deterioration in the coronary circulation.

*S. W. Waydenfeld*

1452. **Chronic Pernicious Myocarditis**
I. K. KLINE and O. SAPHIR. *American Heart Journal* [*Amer. Heart J.*] **59**, 681–697, May, 1960. 8 figs., 24 refs.

Both Kelle in 1892 and Fiedler in 1899 described a disease entity localized to the myocardium. In 1931 Boikan reviewed these and other cases and suggested the name " pernicious myocarditis " and this term has been adopted by the authors of this study from the Michael Reese Hospital, Chicago, because it is an apposite description and has also prognostic usefulness, but they stress that no aetiological unity is implied. Pernicious myocarditis is characterized clinically by relentlessly progressive myocardial insufficiency with an invariably fatal outcome, and pathologically by chronic active interstitial myocarditis. One important known cause is chronic infection with *Trypanosoma cruzi* (Chagas's disease), which should always be first excluded when a chronic pernicious form of myocarditis is encountered in countries where this infection is endemic. Myocarditis of pernicious type has also been reported following pertussis and measles, but most commonly it is an isolated myocarditis occurring without known cause.

The authors have therefore studied some 2,650 recent necropsy records and out of 225 recorded cases of myocarditis found 6 to be of chronic pernicious type. In addition they collected from the literature 23 cases which could in retrospect be reclassified as examples of chronic pernicious myocarditis. The relevant data from these 23 cases are tabulated, while the 6 cases mentioned above are described in detail and form the basis of the study. The patients' ages ranged from 8 to 50 years and the duration of the illness from about 5 weeks to 6 years. One had a history of alcoholism for 2 years before the onset of symptoms, an 8-year-old girl suffered from fatigue and dyspnoea dating from pertussis 2½ years earlier, and a young woman aged 20 had had hepatitis one year before the onset of symptoms; this last patient was the only one with angina. There was no history of hypersensitivity or of rheumatism in any of the cases, and the blood pressure was normal in all. Tachycardia, despite a normal or only slightly raised temperature, was noted in 4 cases, the pulse pressure was low in 3, and arrhythmias were common, varying atrio-ventricular block, multifocal ectopic beats, atrial flutter and fibrillation, and ventricular tachycardia all being seen; individual patients often showed many changes of rhythm. Cardiac failure was invariable and progressive, though often showing temporary remission. The heart was enlarged in all cases and gallop rhythm was noted in 2. Apical diastolic murmurs were misleading and led to a diagnosis of mitral stenosis in 2 cases, while non-specific systolic murmurs were reported in another 3.

At necropsy all showed evidence of chronic cardiac failure, often with anasarca. In no case was there any other disease which might have been associated with myocarditis. Cardiac dilatation and hypertrophy was uniformly present, the hearts weighing from 330 to 460 g. In every case the pericardium and endocardium were normal, the valves were intact, and the coronary arteries could not be incriminated. Mural thrombi in the right atrial appendage were found in 2 cases, in one of which there were pulmonary emboli. The myocardium varied widely in appearance, from normal, through pale and flabby, pale and firm, to mottled. Occasionally some macroscopic streaky fibrosis could be seen. Microscopically there was a true chronic myocarditis, with interstitial infiltration of lymphocytes and histiocytes, young connective tissue compressing and eventually replacing myocardial fibres, while strands of old fibrosis were apparent. Attention is drawn to the difference between pernicious myocarditis—a progressive disease with a continuing active inflammatory process—and myocardial fibrosis, the healed end-result of a true acute myocarditis. Of the 225 cases of myocarditis discovered in this study none of the 39 with endocardial involvement ran a pernicious course.

The authors conclude that the evidence from this study suggests that the most common types of myocarditis which may be classified as pernicious are those of chronic isolated myocarditis and Chagas's myocarditis. Attention is drawn to the close similarity of these two conditions, both in their clinical course and myocardial histology. However, in Chagas's myocarditis trypanosomes of leishmanial form can be seen in the myocardium, but no organism has yet been identified in cases of chronic pernicious myocarditis. The literature is discussed. *Celia Oakley*

## DISTURBANCES OF RHYTHM AND CONDUCTION

1453. **The Cause of Fibrillation**

J. H. Burn. *British Medical Journal* [*Brit. med. J.*] **1**, 1379–1384, May 7, 1960. 48 refs.

The circus movement theory of auricular fibrillation has now been replaced by the concept that fibrillation results from a rapidly discharging ectopic focus. From the University of Oxford the author describes a method of inducing fibrillation experimentally in the atria of a dog heart–lung preparation, in which the preparation is perfused with acetylcholine and the atria stimulated for 30 seconds with square pulses of 1 mA. lasting 0·75 m. second at a frequency of 800 per minute. Fibrillation continued from the cessation of stimulation until perfusion with acetylcholine was stopped. Acetylcholine derivatives did not have a similar effect on the stimulated ventricles of the isolated rabbit heart, probably, it is suggested, because acetylcholine shortens atrial but not ventricular action potentials and therefore the respective refractory periods. Both hypokalaemia and hyperkalaemia facilitated auricular fibrillation, whereas hypothermia abolished it. Ventricular fibrillation in the isolated rabbit heart was facilitated by hypoxia, hypoglycaemia, metabolic inhibitors, and hypocalcaemia, all these states serving to shorten the refractory period and thus permit the spread of impulses from an ectopic focus. *D. Goldman*

1454. **A Surgical Approach to the Management of Heart-block Using an Inductive Coupled Artificial Cardiac Pacemaker**

L. D. Abrams, W. A. Hudson, and R. Lightwood. *Lancet* [*Lancet*] **1**, 1372–1374, June 25, 1960. 4 figs., 6 refs.

Complete heart-block may be symptomless, or disabling because of low cardiac output, or a threat to life itself because of repeated Stokes–Adams seizures; when life is threatened the use of an artificial pacemaker is indicated. In this paper from the Queen Elizabeth Hospital, Birmingham, the authors present a preliminary report of 3 cases of non-surgical acquired heart-block for which they first employed the Lillehei method, in which electrodes are sutured into the ventricular muscle and connected through the chest wall to a pacemaker.

As this method is unsuitable for permanent use they subsequently devised their own externally applied, inductive, coupled artificial cardiac pacemaker by means of which painless control of the heart rate through the intact skin can be successfully maintained. This apparatus consists of a nylon-embedded 3-cm. induction coil buried in the left pectoral muscle over the second intercostal space, the ends of the coil being continued as nylon-covered stainless steel wires which are fixed to the ventricular muscle, the whole constituting the secondary circuit. The primary circuit, a similar 5-cm. coil, is attached to the skin over the buried coil and is supplied by a portable transistor pulse generator which produces short controlled electrical impulses varying from 30 to 100 per minute; from this primary circuit pacemaking pulses of the desired frequency and intensity can be induced in the secondary coil. The application and advantages of this ingenious device are discussed, together with clinical details and brief histories of the 3 cases treated. *C. A. Jackson*

1455. **Disorders of Rhythm and Conduction in Myocardial Infarction.** (Los trastornos del ritmo y de la conducción en el infarto miocárdico)

A. de Micheli, E. Piccolo, F. Cocco, A. Bisteni, and D. Sodi-Pallares. *Archivos del Instituto de cardiología de México* [*Arch. Inst. Cardiol. Méx.*] **30**, 151–167, March–April [received July], 1960. 4 figs., 22 refs.

The authors have studied the incidence and significance of disturbances of rhythm and conduction in 400 patients admitted to hospital with acute or subacute myocardial infarction, and kept under observation for 2 to 3 months. There were 338 men and 42 women ranging in age from 24 to 83 years. In 177 patients (44·45% of the total) disturbances of rhythm and/or conduction were observed. These included 153 (45·27%) of the men and 24 (38·71%) of the women. In 75 cases (18·75%) there was a disturbance of rhythm, in 61 (15·25%) a disturbance of conduction, and in 41 (10·25%) a disturbance of both. Among

the 62 patients who died the incidence of such disturbances was 62·9%.

It became clear that such disturbances were true complications of myocardial infarction. Auriculo-ventricular block, whether of second degree or complete, showed a definite association with infarction of the diaphragmatic surface. It is suggested that in such cases defective blood supply to the A–V node from a branch of the posterior descending branch of the right coronary artery is responsible for the block. A similar association was found between septal infarction and bundle-branch block. On the other hand the various types of arrhythmia observed did not seem to bear such an exact relationship to the site of the infarction, possibly because the ectopic focus in such cases has been shown experimentally to be situated at some point at the margin of the necrotic tissue determined by local differences in tissue electrocyte content. Generally it was possible at most to locate the source of ventricular extrasystoles in one or other ventricle, and, in some cases, to indicate whether such a focus was placed high or low in the ventricle. However, when ventricular extrasystoles or ventricular paroxysmal tachycardia arose in the postero-superior region of the interventricular septum it was possible to indicate the site exactly. Disturbances of rhythm and conduction occurred most frequently during the first week after infarction. The authors state that paroxysmal ventricular tachycardia and complete A–V block had a particularly bad prognosis. *A. C. F. Green*

## CORONARY DISEASE AND MYOCARDIAL INFARCTION

1456. **Anticoagulant Treatment with Sodium Warfarin in Cardiology.** (Le traitement anticoagulant par la warfarine sodique en cardiologie)
M. Mouquin, R. Sauvan, J. Richon, M. Samama, F. Liozon, and P. Leborgne. *Presse médicale* [*Presse méd.*] **68**, 1079–1082, June 4, 1960. 6 figs., 10 refs.

This paper from the Hôpital Broussais, Paris, reports observations on 63 patients with various cardiovascular diseases who were treated with the anticoagulant " warfarin " sodium, the series including 22 with myocardial infarction, 13 with severe angina, 17 with other cardiovascular disorders (including 6 with mitral disease) and 11 with thrombo-embolic complications. These patients were treated for periods of up to 10 months, to a total of 2,710 treatment days, that is, an average of 43 days per patient. The initial treatment consisted of one dose of 40 to 50 mg. of warfarin, and this resulted in the prothrombin time (by the Quick test) falling to between 15% and 35% (the therapeutic zone) within 48 hours in two-thirds of the patients. Following this the daily dose was adjusted according to the prothrombin time, which was estimated daily during the first week, three times in the 2nd week, then twice weekly until the 6th week, and thereafter once every one or two weeks. The usual maintenance dose was found to be between 5 and 12 mg., but smaller doses sufficed in patients who were over the age of 70.

The authors found that warfarin was easily administered in single daily oral doses, that complications and evidence of toxicity were rare, and that absorption and the effect of the drug on the clotting time were fairly consistent. The prothrombin time of patients receiving warfarin correlated closely with the results of other tests for diminished blood clotting, such as the heparin tolerance test, plasma clotting time in silicone tubes, " the Howell time ", and thromboelastography. When the treatment was stopped the prothrombin time began to return to normal in 3 or 4 days and more rapidly if vitamin K was given. On the basis of these observations a scheme for anticoagulant therapy is presented.
*C. Bruce Perry*

1457. **Symmetrical Gangrene Associated with Coronary Thrombosis**
L. D. Wilcox. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **82**, 1066–1072, May 21, 1960. 4 figs., 11 refs.

In this communication from the University of Western Ontario, London, Ontario, the mechanisms causing gangrene of the toes or feet after myocardial infarction are reviewed and a number of clinical examples presented and illustrated. The commonest cause of the gangrene is probably the prolonged shock that follows the infarction, which with its compensatory hypotension and vasoconstriction initiates ischaemia; after this thrombosis in the limb arteries may follow. Two cases, in a man of 75 and a woman aged 62, in which gangrene followed hypotension of 4 or more days' duration, are described.

Intraventricular thrombosis may, at any time in the first 2 or 3 weeks after infarction, cause either saddle embolism at the aortic bifurcation or a series of smaller emboli in the leg arteries. A predilection for the anterior tibial artery rather than the posterior may be due to the size of the vessel and the angle of bifurcation of the popliteal artery. Emboli may also arise from atheromatous material forming in the aortic wall. Finally there may be primary thrombosis in the lower aorta in the absence of severe hypotension, this being possibly due to an increased clotting tendency. Primary thrombosis in smaller vessels may also be found in association with polycythaemia. The author points out the need for effective anticoagulant therapy in the prophylaxis of gangrene, and for prompt surgery in cases of saddle embolus. Although the incidence of gangrene following coronary thrombosis is at present low, it seems likely that with the increased expectancy of life this complication may be met more frequently. *J. A. Cosh*

1458. **Clinical Picture of the Transitional Form of Acute Coronary Insufficiency.** (К клинике переходных форм острой коронарной недостаточности)
L. B. Šimeliovič. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **38**, 81–85, June, 1960. 1 fig., 11 refs.

In the transitional form of acute coronary insufficiency the ischaemia of the myocardium is more intense than that in simple angina, but insufficiently severe to produce an infarct. A series of 33 cases is reported. There was

no obvious precipitating factor in 19 cases; of the remainder, the pain developed while walking in 4, during normal activity in 17, and at rest in 12. The onset was marked by angina in most cases, transient loss of consciousness in one, and unaccountable weakness in 2. The acute period (up to 25 attacks in 24 hours) lasted for 2 to 12 weeks. In patients with a history of simple angina the onset of the transitional form was marked by a change in the character of the attacks and absence of response to nitrites. There were variable changes in the blood pressure, and evidence of tissue necrosis (leucocytosis with a shift to the left, slight pyrexia, and raised erythrocyte sedimentation rate) was found in 12 cases. One patient developed extrasystoles and another a paroxysm of auricular fibrillation. In all cases the electrocardiogram (ECG) showed evidence of myocardial ischaemia, and an increase of the P–R interval was observed in 3.

Routine treatment (bed rest, sedation, vasodilators, and application of leeches) was not always satisfactory. In the absence of absolute contraindications anticoagulants should always be employed. Clinical improvement, though not reflected in the ECG, is observed as soon as the prothrombin index is reduced to between 60 and 70%. The younger the patient, the more complete is recovery likely to be. Of the present patients 8 made a good recovery and the ECG returned to normal in 19. One patient died. In most cases the patient was left with angina of effort, but myocardial function was little affected. It is emphasized that this condition must be treated with the same sense of urgency as frank myocardial infarction. *S. W. Waydenfeld*

1459. **The Physiological Basis and the Results of Treatment of Chronic Coronary Insufficiency by Bilateral Ligation of Internal Mammary Artery.** (Физиологические обоснования и результаты лечения хронической коронарной недостаточности при помощи двусторонней перевязки внутренней грудной артерии)
V. I. Kolesov. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **38**, 71–77, June, 1960. 2 figs., 9 refs.

Ligation of the internal mammary arteries at the level of the 2nd and 3rd intercostal spaces results in an increase of the blood pressure in the proximal segment of the arteries by 10 to 15 mm. Hg. The increased flow is directed to the pericardio-phrenic and pericardial vessels and thus part of it reaches the myocardium. This operation has been performed (under local anaesthesia) on 180 patients with chronic coronary insufficiency and angina pectoris, of whom 110 have been followed up for 4 to 24 months. The latter group was made up of 79 men and 31 women aged 42 to 70 years with disease of 3 to 10 years' duration. There was definite electrocardiographic (ECG) evidence of coronary disease in all cases, and 52 patients had a history of myocardial infarction (2 or 3 attacks in 10 cases). Hypertension was present in 39 cases and circulatory failure in 11. The clinical picture was further complicated in 2 cases by attacks of cardiac asthma and in 2 others by attacks of paroxysmal tachycardia. In all cases conservative treatment had failed or produced only a short-lived improvement, and any other operative procedure was contraindicated. It is emphasized that proper psychological preparation of the patient and good after-care are all-important.

The immediate results (up to 2 months after the operation) were as follows: complete suppression of anginal attacks in 56 cases; reduction in frequency of attacks in 43; and no change in 11. Favourable ECG changes were observed in 40 cases, unfavourable changes in 2, and no change in 68. During the period of follow-up 42 patients remained free from attacks; 48 patients still experienced attacks, but in spite of an increase in the amount of exertion permitted they were less in frequency, severity, and duration. There was no change in 20 cases. ECG improvement was observed in 47 cases. The operative mortality was *nil*, but 5 patients died some months after the operation as a result of the basic condition itself. The author advocates ligation of the pericardio-phrenic artery in those patients in whom bilateral ligation of the internal mammary artery has failed to produce any improvement. This procedure, however, is still in the experimental stage.

*S. W. Waydenfeld*

## BLOOD VESSELS

1460. **Observations on Arteriolar Disease in Arteriosclerosis Obliterans**
D. E. Strandness Jr., D. L. Nothstein, J. A. Alexander, and J. W. Bell. *Surgery* [*Surgery*] **47**, 953–958, June, 1960. 7 figs., 11 refs.

It has been observed in cases of arteriosclerosis obliterans that extensive involvement of the large and medium-sized arteries may occur without clinical evidence of disease. Moreover, the relationship between the location of a major arterial obstruction and the site of necrosis of the tissues is often not constant. The probability that arteriolar disease may play a part in the genesis of local tissue death must therefore be considered, and with this in mind the pathological changes in the arterioles were studied, " with the full realization that the physiological consequences of anatomic changes can be only inferred ", at the Veterans Administration Hospital and University of Washington School of Medicine, Seattle, in limbs amputated from 15 patients with arteriosclerosis obliterans and one with Buerger's disease. The patients, 15 men and one woman, ranged in age from 43 to 72 years. Eight of them had diabetes mellitus. The indications for amputation were ulceration and gangrene in 15 cases and pain in the remaining case. The changes in the major vessels were studied both radiographically and microscopically. In addition sections for histological study of the arterioles were taken in a systematic manner from the areas supplied by the major arteries and included skin, subcutaneous tissue, and muscle. All areas showing ulceration and gangrene were avoided.

Definite arteriolar changes were frequently observed in the cases of arteriosclerosis obliterans, the principal lesions noted being intimal proliferation and hyalinization of the muscular media. (These changes were not

found in the case of Buerger's disease.) The severity of involvement of the arterioles varied and seemed to bear no direct relationship to the degree of involvement of the major arteries. It was impossible to determine whether the arteriolar changes preceded, followed, or coincided with the arterial changes.

It is suggested that the degree of arteriolar change present in cases of arteriosclerosis obliterans may affect the response to lumbar sympathectomy and to angioplastic procedures.

[This is an informative short paper. Our knowledge of this subject can be advanced only by closer cooperation between surgeons and pathologists, especially in the examination of amputated segments of limbs.]

*Leon Gillis*

1461. **Role of Fibrinolytic Agents in Thrombotic Diseases**
R. V. CHAPPLE and H. O. SINGHER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **173**, 221–225, May 21, 1960. 1 fig., 17 refs.

After reviewing the theoretical and experimental background to the therapeutic use of fibrinolysin in thrombotic diseases the authors discuss the clinical effects of fibrinolysin treatment as seen in 400 cases of various circulatory disorders, including cerebral thrombosis, cerebral embolism, thrombotic and embolic disease of the peripheral and splanchnic arterial systems, pulmonary embolism, and venous thrombosis. [The details of these cases were apparently collected from a number of different sources, which are not specified.] A moderate and transient depression of the fibrinogen content of the blood was observed, but no haemorrhage occurred. A short-lived rise in temperature was common, but could be countered by the administration of antipyretics, antihistaminics, or sedatives. Urticarial reactions occurred in less than 1% of patients. Of 171 cases of thrombophlebitis of a limb in which the relevant data were available, a satisfactory response, defined as the return of the limb to normal size within 48 to 72 hours, was obtained in 65%, a variable degree of improvement in 26%, and no response in 9%. Further analysis of the data indicated that, as would be expected, a good response was obtained more readily when treatment was started within 5 days of the clotting episode than when it was delayed beyond this period.

Finally the results of treatment with anticoagulants and fibrinolysin in 20 cases of deep thrombophlebitis of the leg are compared retrospectively with those of treatment with anticoagulants only in a group of 22 similar cases. The fibrinolysin used was a preparation of human material (" actase ") and the anticoagulant therapy consisted of heparin followed by dicoumarol. [Dosage is not stated.] The selection of patients and evaluation of response were based on a number of rigid criteria, which are defined. In 10 of the cases in the first group treatment with fibrinolysin and anticoagulant was started simultaneously; in these, discomfort disappeared in one to 5 (average 2·8) days, and swelling in one to 4 (average 2·0) days. The remaining 10 patients in this group were treated with fibrinolysin after one to 9 days of anticoagulant therapy, usually without response; discomfort disappeared in one to 4 days in 9 of these and in 8 days in the tenth, while swelling cleared in one to 4 days in 7, but was still present after 8, 18, and 19 days respectively in the other 3. In the 22 patients treated with anticoagulants alone discomfort disappeared in 2 to 14 (average 6·0) days and swelling in 2 to 10 (average 5·2) days.

The authors conclude that the use of fibrinolysin in conjunction with anticoagulants decreases the morbidity in patients with thrombophlebitis. Brief reference is also made to increased speed of recovery with fibrinolysin therapy in patients with pulmonary embolism, in which, however, accurate methods of diagnosis and therapeutic evaluation are not available.

[This article unfortunately lacks the succinct approach, and one feels that closer adherence to the conventional mode of writing a scientific paper would have enabled the reader to learn even more of the careful work behind it.]

*J. Warwick Buckler*

1462. **Anticoagulant Drugs in the Treatment of Pulmonary Embolism: a Controlled Trial**
D. W. BARRITT and S. C. JORDAN. *Lancet* [*Lancet*] **1**, 1309–1312, June 18, 1960. 11 refs.

Soon after the first use in 1937 of an anticoagulant drug in the treatment of venous thrombosis claims began to be made that this treatment reduced the incidence of fatal pulmonary embolism. In the controlled trial here reported from the United Bristol Hospitals, the object of which was " to measure the effect of anticoagulants in patients who have had one pulmonary embolism, both on the course of the first embolism and on the risk of further attacks ", patients in whom pulmonary embolism was diagnosed were, provided there was no contraindication to the use of anticoagulants, allocated to an " anticoagulant " or " no anticoagulant " group by the drawing of a card. The two groups were treated similarly, except that one received the anticoagulants heparin and nicoumalone (" sinthrome ") for 14 days.

When 35 patients had been admitted to the trial a review of the results at that time showed that of 19 patients who had not received anticoagulants 5 had died of pulmonary embolism and a further 5 had suffered another but non-fatal embolism, whereas of the 16 who had received anticoagulants none had died of pulmonary embolism (one, however, died of suppurative pneumonia and intestinal haemorrhage) and there was no case of recurrence. It was considered unjustifiable to continue the trial in its original form and all subsequent patients (a further 38) admitted to the study received anticoagulants. The trial was stopped when a total of 54 patients had been so treated. Among the additional 38 patients there was one further death (not due to pulmonary embolism) and one non-fatal recurrence. Brief histories of the 7 fatal cases in the series are presented. The authors suggest that it seems reasonable to conclude that even after embolism has reached the pulmonary arteries anticoagulant therapy reduces the risk of death from heart failure or from pulmonary infarction and also of recurrent embolism. Further, in untreated patients deaths from pulmonary embolism are likely to outnumber the deaths that may be attributed to anticoagulant treatment.

*G. Clayton*

## SYSTEMIC CIRCULATORY DISORDERS

1463. **Recovery from Hypertensive Disease.** (Обратное развитие гипертонической болезни)
A. V. Kolosov and N. K. Beljaeva. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **38**, 19–24, June, 1960. 1 fig., 11 refs.

Little is known about the chances of complete recovery from hypertensive disease as distinct from remissions induced by such occurrences as myocardial infarction or cerebrovascular accident. In an attempt to elucidate this question the authors have followed up 300 hypertensive patients, 205 above and 95 below the age of 40, for periods up to 10 years. Patients showing any tendency to remission induced by another pathological process were excluded. The prophylactic measures applied included attention to the way and standard of life and nutrition, adjustment of work, and recuperative holidays. The majority of the 197 patients with hypertension of Stages I and IIa responded well to this treatment alone, but some required short courses of hypotensive drugs or sedatives and 17 had to be admitted hospital. The 103 patients in Stages IIb and III, however, all received repeated courses of hypotensive drugs sedatives, or hormones. The clinical course of the disease during the period of observation was defined as complete recovery (absence of symptoms with normal blood pressure for at least 5 years), regression (with recession of the manifestations of the disease to those of an earlier stage), improvement (objective and subjective), stabilization (no deterioration), deterioration, or death.

Of 112 patients in Stage I, 68 recovered, 40 became stabilized, and only 4 deteriorated and progressed to Stage II; of 85 in Stage IIa, 11 recovered, 13 regressed, 7 improved, 47 remained stable, and 11 deteriorated; of 63 in Stage IIb, none recovered, one regressed, 9 improved, 35 became stabilized, 15 deteriorated, and 3 died; and of 40 in Stage IIIa, 20 showed some evidence of improvement or stabilization, 10 deteriorated, and 10 died. It is therefore concluded that comprehensive therapeutic and preventive measures can be relied upon to produce good results only in the early stages of the disease, and great stress is laid on their early employment.

*S. W. Waydenfeld*

1464. **Studies on a New Hypotensive Agent: Bretylium Tosylate**
J. Genest, C. Dufault, G. Pigeon, J. Davignon, P. Biron, and J. Trudel. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **82**, 872–877, April 23, 1960. 9 figs., 6 refs.

From the Hôtel-Dieu Hospital, Montreal, the results are reported of the treatment of 41 hypertensive patients with bretylium tosylate for periods varying from 3 to 29 weeks. In the milder cases the drug was given alone in an average daily dose of 725 mg. (range 300 to 1,200 mg.); in more severe cases chlorothiazide was given concomitantly, and in 3 very severe cases hydrallazine was also administered. Bretylium tosylate produced a satisfactory fall in blood pressure in the upright position, which was particularly marked when chlorothiazide was also administered. In regard to side-effects 12 patients complained of dizziness and excessive fatigue in the upright position, orthostatic hypotension occurred in 10 others, while 9 patients had mild digestive disorders and 4 complained of pain in the jaw muscles when eating. Two patients died during treatment [but the cause of death is not stated]. The authors stress the effectiveness of bretylium tosylate and its almost complete absence of parasympathetic blocking action.

*Bernard Isaacs*

1465. **Clinical Experience with Bretylium Tosylate**
J. A. Lewis. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **82**, 877–881, April 23, 1960. 2 figs., 11 refs.

At the Westminster Hospital, London, Ontario, 10 hypertensive patients were treated successfully with bretylium tosylate. Satisfactory reduction of the blood pressure in the standing position was obtained, with freedom from side-effects attributable to parasympathetic blockade. Unlike other workers the present author did not find that the addition of chlorothiazide and hydrallazine enhanced the hypotensive effect of bretylium [but such a combination was employed in only 3 cases].

*Bernard Isaacs*

1466. **Electrocardiographic Changes in Essential Hypertension.** (Considerazioni sulle alterazioni elettrocardiografiche nell'ipertensione arteriosa essenziale)
C. Giusti. *Folia cardiologica* [*Folia cardiol.* (*Milano*)] **19**, 223–238, June 30 [received Sept.], 1960. 4 figs., 34 refs.

1467. **Vascular Responses to Smoking Tobacco Compared with Responses to Skin Testing of Tobacco Extracts**
K. de Crinis, W. Redisch, V. Fontana, A. Lewis, M. B. Sulzberger, and J. M. Steele. *Annals of Internal Medicine* [*Ann. intern. Med.*] **52**, 1035–1041, May, 1960. 27 refs.

From New York University College of Medicine the authors report the results of an investigation into the effects of smoking on the cardiovascular system of 80 healthy smokers, 27 women and 53 men ranging in age from 18 to 50 years, these effects being then compared with the results of skin tests carried out with the dried extracts of each of the various tobaccos used in the test cigarettes.

In 28 of the subjects smoking produced a significant fall in peripheral blood flow, as measured by a plethysmograph applied to the leg and foot, but in only 11 was there a significant fall in surface temperature; a further 10 subjects showed changes in the ballistocardiogram, and 3 in the electrocardiogram. A positive skin reaction to the tobacco extract was given by 32 subjects and of these, 21 had shown some circulatory changes after smoking. On the other hand, of the 48 subjects in whom the tobacco skin test was negative 43 also showed no changes in the circulation after smoking. The authors state that further similar investigations are to be carried out in healthy non-smokers and in both smoking and non-smoking patients with peripheral arterial disease.

*H. F. Reichenfeld*

# Clinical Haematology

1468. **Anaemia in a Group of Elderly Patients.** [In English]
I. R. LAWSON. *Gerontologia clinica* [*Geront. clin. (Basel)*] **2**, 87–101, 1960. 7 figs., 21 refs.

In this paper from Woodend General Hospital, Aberdeen, the author reports a study of 102 anaemic patients out of 319 admitted to the geriatric unit, all of them being aged over 60 years; those with known malignant disease were excluded. It was found that 72 patients showed a normoblastic marrow. Estimation of the bone marrow haemoisiderin content in these patients (by methods described) showed that iron was not lacking. The patients with this type of normoblastic anaemia could be divided into two groups: (1) 33 with rheumatoid arthritis, renal failure, or other causes known to predispose to similar types of anaemia in younger people; and (2) 39 cases in which the predominant cause of the anaemia was infection.

Iron-deficiency anaemia with depressed marrow iron content was apparent in only 12 patients, 5 men and 7 women. In the male patients it was invariably associated with recent blood loss; in the women, however, iron-deficiency anaemia could only be partly attributed to this cause for only 3 out of the 7 showed evidence of gastro-intestinal bleeding. The author concludes that iron-deficiency anaemia is an unusual cause of the low haemoglobin level found in elderly patients. This conclusion, which differs from that of many other workers, is discussed. The author deprecates the indiscriminate administration of iron to old people, since not only is it in many cases inappropriate to the cause of the anaemia, but in the presence of true iron deficiency may mask early evidence of a remediable neoplasm.

*I. McLean Baird*

1469. **Primary Hemorrhagic Thrombocythemia**
F. L. OZER, W. E. TRUAX, D. C. MIESCH, and W. C. LEVIN. *American Journal of Medicine* [*Amer. J. Med.*] **28**, 807–823, May, 1960. 9 figs., bibliography.

Since it was first described by di Guglielmo in 1920 the syndrome characterized by haemorrhage and thrombocythaemia has been reported in the literature under a variety of names. Writing from the University of Texas Medical Branch, Galveston, the present authors report their experience with 6 (or possibly 7) cases of this syndrome, review the literature, and propose certain diagnostic criteria. With one exception—a girl aged 12 who ultimately developed acute myeloblastic leukaemia—the patients ranged in age between 48 and 60, 4 being women and 2 men.

The symptoms were mainly related to thrombohaemorrhagic phenomena, in particular epistaxis and gastro-intestinal bleeding or purpuric manifestations, but one patient had experienced epileptic seizures of recent occurrence, one a hemiplegia, and one symptoms of carotid artery insufficiency. Paraesthesiae of the extremities were reported by 3 patients, while pressure symptoms due to hepato-splenomegaly were prominent in 2. The chief signs were related to the thrombohaemorrhagic phenomena and anaemia when present. Splenomegaly was present in all the patients but lymphadenopathy was not found in any. The principal laboratory findings were a raised platelet count varying between 1,000,000 and 6,000,000 per c.mm.. abnormal platelet morphology, and hyperplasia of all marrow elements, especially the megakaryocytes and megakaryoblasts. A coagulation defect was found in one patient. In the presence of anaemia the stools were always guaiac-positive but a definite source of bleeding could never be demonstrated. Radioactive phosphorus was given to 6 patients and resulted in haematological and clinical remissions lasting for periods varying from 5 to 13 months. One patient was given nitrogen mustard because of the acuteness of her condition, but this produced no amelioration and she died.

In the literature 48 cases of this syndrome have been described, but in the authors' view only 23 of these can be regarded as true examples of primary haemorrhagic thrombocythaemia if the following criteria are taken as diagnostic: (1) a history of thrombo-haemorrhagic phenomena; (2) the presence of an enlarged spleen; (3) an erythrocyte count of not more than 6,000,000 per c. mm., haemoglobin value not exceeding 18 g. per 100 ml., haemocrit value not above 54%, leucocyte count not exceeding 50,000 per c.mm., and a platelet count persistently above 800,000 per c.mm.; (4) a hyperplasia of all marrow elements with megakaryocyte predominance and platelet masses plus eosinophilia and/or basophilia; and (5) an absence of leukaemic tissue infiltration. The case histories of the 7 cases are described in detail.

*A. Ackroyd*

1470. **Hemorrhagic Thrombocythemia: a Critical Review**
F. W. GUNZ. *Blood* [*Blood*] **15**, 706–723, May, 1960. 5 figs., bibliography.

1471. **Giant Follicle Lymphoma of the Spleen: Recovery after Splenectomy**
R. A. HICKLING. *British Medical Journal* [*Brit. med. J.*] **1**, 1464–1467, May 14, 1960. 38 refs.

The author of this paper from Charing Cross Hospital, London, describes 4 cases of giant follicle lymphoma of the spleen in patients aged 36, 46, 72, and 51 years respectively, all of whom underwent splenectomy with uniformly excellent results.

Giant follicle lymphoma, or Brill–Symmers disease, is usually regarded as a disease of the lymph nodes, many of which, both superficial and deep, are enlarged in

most cases. However, enlargement of the Malpighian bodies in the spleen, which are the equivalent of lymph nodes, also occurs and may cause splenomegaly. In various series of cases reported in the literature the proportion in which splenomegaly was observed has varied from 33 to 64%. A number of cases have also been reported in which only the spleen appeared to be involved, but in some of these enlargement of the lymph nodes appeared later. The disease process does not appear to be a malignant one and does not of itself cause death, differing in this respect from true lymphosarcoma or the leukaemias.

In the 4 cases described the condition appeared to affect chiefly the spleen, enlargement of the superficial lymph nodes being absent, but there were lymphoid changes in the bone marrow in 2 cases and the liver in 3, as shown by biopsy, while in 3 cases enlarged lymph nodes were felt in the abdomen at operation. In the peripheral blood a relative lymphocytosis, with abnormal and immature mononuclear cells, was found, but there was no absolute increase in the leucocyte count. The appearances both in the peripheral blood and the bone marrow were suggestive of aleukaemic lymphatic leukaemia. Splenectomy was carried out in each case primarily because of the discomfort caused by the splenomegaly. All 4 patients made a good recovery, the symptoms disappearing and the blood picture gradually returning to normal. It is suggested that there may be several conditions which cause the histological changes of giant follicle lymphoma and that the cases reported represent one of these, which may be a primary disease of the spleen.

[The references to the literature are numerous and very complete.] *J. W. McNee*

## NEOPLASTIC DISEASES

1472. **Geographical Variation in Leukaemia Mortality in Relation to Background Radiation and Other Factors** W. M. Court Brown, R. Doll, F. W. Spiers, B. J. Duffy, and M. J. McHugh. *British Medical Journal* [*Brit. med. J.*] **1**, 1753–1759, June 11, 1960. 4 figs., 19 refs.

There is strong evidence that exposure to ionizing radiation in high dosage is leukaemogenic, but the risk of exposure to small amounts of radiation over a long period is unknown, although it may be guessed at by extrapolation. Direct observation of the effect of background radiation is very difficult (and, it is admitted, may be impracticable), but it was attempted in the present survey.

Of 10 parts of Scotland investigated, the highest mortality from leukaemia was in Aberdeen (146% of the expected) and the second highest in Edinburgh (124% of the expected). The outdoor and indoor background radiation was measured in four areas, Aberdeen, Aberdeenshire, Edinburgh, and Dundee. A portable high-pressure ionization chamber (S.E. $\pm 1{\cdot}5\%$ for a single observation; ion-collection time 3 minutes) was used and great care was taken to obtain an accurate assessment of the local gamma-ray dose-rate. It was calculated that the highest average marrow dose from background sources is received in Aberdeen with its granite houses (101 m.rad a year), and the lowest in Edinburgh with its sandstone houses (80 m.rad a year). The higher incidence of leukaemia in Aberdeen is thus accompanied by a higher intensity of background radiation. It is calculated, however, that a difference in radiation of this order could account for little more than 1% of the observed difference in mortality—if indeed such doses are capable of being leukaemogenic at all. There were also differences in the predominant type of leukaemia in the two cities, the excessive mortality in Aberdeen being due mainly to acute leukaemia and chronic myeloid leukaemia, whereas chronic lymphatic leukaemia accounted mainly for the excess mortality in Edinburgh. Clearly there must be other factors to account for the high mortality figures for Aberdeen and Edinburgh in comparison with the rest of Scotland. Possible explanations include better case-finding, higher social and economic status, and differences in exposure to diagnostic radiology, although these are not likely to be great.

*R. B. Thompson*

1473. **A Survey of Leukaemia in Cornwall, 1948–1959** E. E. Wood. *British Medical Journal* [*Brit. med. J.*] **1**, 1760–1764, June 11, 1960. 1 fig., 14 refs.

Because of its isolated geographical position and relatively static population West Cornwall was felt to be a suitable area for the study of certain problems relating to the incidence of leukaemia. In view of the lack of diagnostic facilities which existed before 1948 the survey was restricted to the 12 succeeding years, when such facilities have become much more widely available to general practitioners. No evidence was found of a rise in incidence of the disease since 1948. The author stresses the very great importance of better case-finding as a factor leading to an apparent increase in the incidence. A greater awareness both of the frequency of the disease in older age groups (75% of cases diagnosed during the period occurred in patients over the age of 40) and of the atypical features often assumed by the disorder in the elderly has led to the diagnosis being more often made in recent years.

A careful radiometric survey of the area was made and although high local levels of radioactivity, associated with granite outcrops, are known to exist in Cornwall, no significant relationship could be detected between the local incidence of leukaemia and the level of radioactivity. Diagnostic radiology during pregnancy did not appear to be of aetiological importance; none of the children born to a series of 200 women who were x-rayed during pregnancy developed leukaemia—indeed the incidence of leukaemia during early childhood appeared to be falling. Only one mother of a leukaemic child (there were 20 in the series) had had an abdominal x-ray examination during pregnancy (at the 35th week). It was noted in several instances that two or more patients living in close proximity developed acute or chronic leukaemia or a related condition within a short time of each other, but there was no significant predominance in any particular district. *R. B. Thompson*

# Respiratory System

1474. **Expired-air Resuscitation**
J. Cox, R. Woolmer, and V. Thomas. *Lancet* [*Lancet*] 1, 727–730, April 2, 1960. 7 figs., 14 refs.

Expired-air resuscitation was carried out on 22 anaesthetized and paralysed patients undergoing elective surgery, the mouth-to-airway method of Safar being used. The donors were untrained in this technique; the periods of resuscitation ranged from 15 to 115 minutes. Tidal volume was measured by interposing a pneumotachograph head across the airway, this being connected to a differential capacitance manometer, recording on a pen oscillograph. From an adjacent sampling tube, carbon dioxide concentration was continuously analysed with a rapid infra-red analyser. The airway was held against the patient's mouth with a foam plastic seal.

It was found that the patient's end-tidal carbon dioxide concentration could easily be maintained below 5·6% provided the minute volume did not fall below 10 litres. The advantages of the method are its simplicity, it is easy to teach to untrained subjects, and no elaborate apparatus is required (mouth-to-mouth resuscitation can be employed if necessary). *D. Goldman*

1475. **A Study of the Aetiology of Respiratory Disease in a General Hospital**
W. W. Holland, E. I. Tanner, M. S. Pereira, and C. E. D. Taylor. *British Medical Journal* [*Brit. med. J.*] 1, 1917–1922, June 25, 1960. 5 figs., 14 refs.

During the winter of 1958–9 bacteriological and virological investigations were carried out on all patients—179 adults and 117 children—admitted to the medical wards of St. Thomas's Hospital and the Royal Waterloo Hospital, London, suffering from an acute respiratory illness; respiratory disease accounted for more than one-third of all children and 15% of adults admitted. The aetiology of these infections could be determined in about one-quarter of the cases. Thus 28% of illnesses in children and 22% of illnesses in adults were associated with an identifiable virus, most commonly the viruses of influenza A and B. Three different strains of influenza-A virus, all Asian, were isolated, and serological evidence of infection was obtained in 28 patients, while four strains of influenza-B virus were isolated, serological evidence being obtained in 12 patients, one of whom also had evidence of infection with influenza-C virus. Evidence of virus infection was obtained more commonly in children and adults admitted with an acute illness (33%) than in those with a "chronic" illness (18%). There was no relation between the various pathogens isolated from the sputum or naso-pharynx and evidence of virus infection in the patients.

Nose and throat swabs were taken at intervals of 2 days from 62 (53%) of the children and 103 (61%) of the adults. During their stay in hospital (average 6 days for children and 9 days for adults) 6 of the children (10%) and 17 of the adults (17%) retained the same phage type of *Staphylococcus aureus* throughout, 13 (21%) of the children and 11 of the adults lost the original strain without acquiring a new phage type, while 15 children (24%) and 32 adults acquired a new strain of staphylococcus in the naso-pharynx. However, 28 children (45%) and 43 adults (42%) did not acquire a strain of *Staph. aureus* throughout their stay in hospital. Those strains which were acquired were usually resistant to more than one antibiotic. There were no deaths among the children, but 12 adults (6·7%) succumbed. In 3 of the 5 adults who came to necropsy a hospital-acquired strain of *Staph. aureus* was demonstrated. *H. Caplan*

1476. **Pneumonia with Antibodies to *Streptococcus* MG**
T. B. Anderson. *Lancet* [*Lancet*] 1, 1375–1378, June 25, 1960. 1 fig., 9 refs.

The author describes 20 cases of atypical pneumonia, seen in general practice in Cambridge, which he designates "*Streptococcus* MG pneumonia" without necessarily implying that *Streptococcus* MG is the cause of the disease. It behaves like an atypical pneumonia in that there is a definite interval between the onset of symptoms and the physical signs found in the lungs. The onset is usually "influenzal" in character, with fever, headache, and limb pains. Few abnormal signs are to be found in the upper respiratory tract. The leucocyte count is normal or subnormal in the early stages and a leucocytosis developing later is indicative of a secondary infection. Radiography usually shows a bronchopneumonic type of lesion; in only one of the author's cases did a pleural effusion develop. Antibodies to *Streptococcus* MG appear from the 7th day onwards. The differential diagnosis is from influenza, measles before the rash appears, adenovirus infection, lobar pneumonia, bacterial bronchopneumonia, and pertussis. It is significant that in the author's practice, of 124 cases of lower respiratory-tract infection investigated serologically, antibodies to *Streptococcus* MG were found in 21. Antibiotics have no specific effect on this type of pneumonia, but they undoubtedly control secondary infection and for this purpose the tetracyclines are probably the best. Two illustrative case histories are described in detail and various theories of causation are discussed.
*Paul B. Woolley*

1477. **Carcinoma of the Bronchus Presenting with Gastro-intestinal Symptoms**
E. J. M. Weaver and R. H. Balme. *British Medical Journal* [*Brit. med. J.*] 1, 1543–1545, May 21, 1960. 2 figs., 7 refs.

This paper draws attention to the fact that of 333 patients with carcinoma of the lung admitted to the London Hospital between June, 1956, and July, 1958, 17 (5%) presented with gastro-intestinal symptoms only.

Examination showed that these 17 patients fell into two groups: (1) 5 who had peptic ulceration of the stomach or duodenum as well as carcinoma of the bronchus, and (2) 12 who showed no evidence of peptic ulceration. Of the 17 cases 13 were treated by resection, undergoing either pneumonectomy or lobectomy. Of the remaining 4, 2 were found to have inoperable lesions at thoracotomy and in 2 surgery was not attempted, spinal metastases being present in one and pleural involvement in the other.

The authors remark that it is surprising that the co-existence of bronchial carcinoma with peptic ulcer in the same patient has not previously been the subject of comment, since both peptic ulcer and bronchial carcinoma are common in middle-aged men who smoke cigarettes. However, such a combination is not the complete explanation since 12 of the authors' patients showed no peptic ulceration and at least 2 had given up smoking 5 and 2 years respectively before the appearance of the abdominal symptoms. A small primary carcinoma may influence distant organs by the release into the blood stream of some active principle or by removing some essential nutrient. Such a humoral mechanism must operate to produce the well-known systemic effects manifested by anaemia, cachexia, fever, neuropathy, myopathy, and migrating thrombophlebitis, and thus could possibly also have been responsible for the gastro-intestinal symptoms in some of these cases. On the other hand, however, in 9 of the 17 cases the vagus nerve was surrounded by the growth, though the nerve was not actually invaded. In these cases chronic irritation of the vagus would be expected to produce gastro-intestinal symptoms. The authors conclude: "Whatever the mechanism involved, the coexistence of bronchial carcinoma and dyspepsia poses a diagnostic problem. Error is particularly likely when the only symptoms are gastro-intestinal, a peptic ulcer is demonstrated, and routine chest x-ray examination shows minimal changes of doubtful significance." *Kenneth M. A. Perry*

1478. **Smoking and Personality**
H. J. EYSENCK, M. TARRANT, M. WOOLF, and L. ENGLAND. *British Medical Journal* [*Brit. med. J.*] **1**, 1456–1460, May 14, 1960. 1 fig., 18 refs.

The study here reported was undertaken by Mass-Observation, Ltd., on behalf of the Tobacco Manufacturers' Standing Committee to test the hypothesis that there might be genotypic differences between persons with different smoking habits. On theoretical grounds it was postulated that smoking habits would be positively related to extraversion and neuroticism and negatively related to the personality trait of rigidity. A questionary was constructed containing 31 questions which had been found previously to provide good measures of these traits and it was planned to put it to 2,400 men divided equally into 2 social grades, 2 age groups (40 to 59 and 60 to 70 years), and 6 smoking categories (that is, 24 groups in all). Subjects were obtained by "quota sampling"—that is, each interviewer was allocated a quota of persons of a given social class, age, and smoking category to be interviewed. The sample was, however, made as representative of the population as possible by selecting areas in which the men were to be interviewed which were representative of geographical regions and of various grades of urbanization. In the event it proved impracticable to obtain 200 non-smokers aged 60 to 70 years and in this age group data were collected only for 70 non-smokers in the upper social grade and 90 in the lower.

A factor analysis was then made of the correlations between the 31 questions and age, social class, and smoking habits. Three clear-cut factors were found which could be identified with the three traits under study and were defined by the answers to specific groups of questions. Scores were calculated for each factor for each individual and the mean scores for each smoking group compared. The mean score for extraversion was found to increase progressively and that for rigidity to decrease progressively from non-smokers to light cigarette smokers, medium cigarette smokers, and heavy cigarette smokers, and the differences between the groups were statistically significant. There was, however, little difference between the scores for neuroticism. Pipe smokers were distinguished from cigarette smokers by all three factors.

Other evidence suggests that extraversion is in part determined by genetic factors and the authors consider that their results "make more reasonable than had previously been the case the proposition that both smoking and cancer may be causally related to certain underlying genotypic factors". *Richard Doll*

1479. **A Review of the Evidence on the Relationship between Smoking and Lung Cancer**
D. F. DAVIES. *Journal of Chronic Diseases* [*J. chron. Dis.*] **11**, 579–613, June, 1960. Bibliography.

1480. **Tracheotomy for Acute Pulmonary Insufficiency Complicating Chronic Pulmonary Emphysema**
L. B. TECIMER and M. L. PEARCE. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **105**, 891–898, June, 1960. 2 figs., 25 refs.

From the Wadsworth General Hospital, Veterans Administration Center, and the University of California, Los Angeles, 4 cases are described to demonstrate the value of early tracheotomy in patients with acute pulmonary insufficiency complicating chronic pulmonary emphysema. In 2 cases the insufficiency followed oversedation with barbiturates, and in another a favourable course was interrupted by severe respiratory distress after the development of viscid and purulent sputum which was extremely difficult to expectorate. The fourth patient, who had had recent surgical treatment for a broncho-pleural fistula which appeared after a spontaneous pneumothorax, required assisted respiration and frequent aspiration of secretions. It is pointed out that in such cases tracheotomy provides an adequate airway, facilitates the removal of secretions, makes assisted respiration more effective, and is almost mandatory if a tank respirator is being used, since it prevents the patient from struggling against the respirator by closing his glottis. *B. Golberg*

# Urogenital System

1481. **Gastrodialysis in the Treatment of Acute Renal Failure**

T. A. MARR, J. M. BURNELL, and B. H. SCRIBNER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **39**, 653–661, April, 1960. 4 figs., 12 refs.

A relatively simple method of regulating the electrolyte content and volume of body fluid, the blood urea level, and the acid–base balance in acute renal failure is described in this paper from the Veterans Administration Hospital and the University of Washington, Seattle. A bag of non-waterproof "cellophane" is attached to a plastic tube and introduced into the stomach through the mouth; it is left in place for several days. The bag is filled with 200 to 800 ml. of a suitable dialysing fluid at 37° C., which is changed every 20 minutes, automatically if possible. Measurement of the volume and constituents of the dialysate returned in 24 hours provides accurate information about the exchanges which have taken place between the gastric juice and the dialysing fluid. With a fluid containing 50 mEq. of sodium per litre and 100 mEq. of chloride per litre there is virtually no transfer of these ions. Potassium ions usually need to be removed and the dialysing fluid therefore contains no potassium. Acidosis can be corrected by adding 100 mEq. of bicarbonate per litre. The amount of non-protein nitrogen removed depends upon the concentration of blood non-protein nitrogen and upon the volume of the dialysate. Water removal is ensured by using a hyperosmolar fluid, and can be regulated by adjusting the dextrose content; 20% dextrose is a suitable concentration, and the patient absorbs about 150 g. of this dextrose in 24 hours.

This method was used in 12 adults and 2 children with acute renal failure for a total of 65 days (2 to 16 days, mean 6 days per patient). Up to 43 mEq. of potassium and a mean of 2 g. of non-protein nitrogen were removed daily. The clinical course appeared to be better than could be expected with conservative management alone and complications were infrequent and not of major consequence. The authors state that gastrodialysis will prevent serious uraemia and hyperkalaemia in those patients without serious infection or trauma and will therefore obviate or reduce the need for haemodialysis by an artificial kidney. *T. B. Begg*

1482. **The Reaction of Subcutaneous Drainage in Anasarca**

D. W. VERE and C. E. KING. *Lancet* [*Lancet*] **1**, 779–787, April 9, 1960. 10 figs., 28 refs.

The authors describe from the London Hospital 10 episodes of circulatory collapse which occurred following the subcutaneous drainage of oedema fluid from 7 patients; 9 of the episodes were in patients with glomerulonephritis. Collapse was associated with oliguria, potassium depletion, and a rising blood urea concentration; the symptoms could be alleviated by giving salt by mouth. The mechanism of this reaction is discussed and a parallel drawn with the "response to injury" reaction. The main cause of the circulatory collapse is thought to be an acute reduction in plasma volume. The dangers of such drainage and measures for their prevention are described.

[The conjunction of the circulatory effects of salt-depletion with persisting peripheral oedema has also been recognized in patients treated vigorously with diuretics while on a low-salt diet.] *D. A. K. Black*

1483. **Hydronephrosis**

H. G. HANLEY. *Lancet* [*Lancet*] **2**, 664–667, Sept. 24, 1960. 1 fig., 16 refs.

1484. **The Nephrotic Syndrome Treated with Cortisone in Intermittent High Dosage**

R. G. MITCHELL. *Lancet* [*Lancet*] **1**, 843–845, April 16, 1960. 1 fig., 17 refs.

At Dundee Royal Infirmary the author has treated 5 nephrotic children, all girls, aged 4½ to 12¾ years with intermittent, high-dosage, corticosteroid therapy. The illness had lasted for periods varying from 9 months to 3 years before this regimen was begun and all the patients had failed to respond to one or more courses of hormone therapy, or had relapsed after a temporary remission. Initially they were given 2 weeks' treatment with corticotrophin (20 mg. twice daily), which led to diuresis and loss of oedema in 4 cases, followed 5 days later by cortisone acetate by mouth in a dosage of 100 mg. every 6 hours for one 3-day period in each week. In the first 3 patients treated the first course lasted only 20 weeks, but their later courses and the initial courses in the other 2 patients were continued for at least one year, at the end of which the intervals between the 3-day courses were gradually lengthened over several months. Treatment was begun in hospital and then maintained on an outpatient basis. Fluids were not restricted and potassium supplements were given only at the time of the initial diuresis; all the patients were given continuous oral penicillin therapy. In 2 cases the regimen had to be adjusted when hypertension developed.

All 5 children had been in a state of chronic invalidism, but on the regimen described they were soon able to resume normal lives and indeed showed remarkable physical well-being and relative freedom from childhood respiratory infections. Three of them have now been in complete remission for 12 to 30 months; in the other 2 treatment has been changed to small daily doses of prednisolone since they were showing occasional traces of proteinuria. The author concludes that despite its relatively high cost intermittent, high-dosage, corticosteroid therapy may be the treatment of choice for childhood nephrosis. *K. G. Lowe*

# Endocrinology

1485. **A Comparison of the 15-Minute Continuous Thyroid Uptake Test with Other Radioiodine Tests**
N. HOWARD, E. O. FIELD, and G. M. DYCHE. *British Journal of Radiology* [*Brit. J. Radiol.*] **33**, 316–320, May, 1960. 3 figs., 11 refs.

In a study undertaken at the Royal Marsden Hospital, London, to assess the value of the 15-minute continuous thyroid uptake test of Larsson and Jonsson (*Acta radiol. (Stockh.)*, 1955, **43**, 81) in the investigation of malignant thyroidal conditions, this test (using a dose of 100 $\mu$c. of radioactive iodine ($^{131}$I)) was compared with the 2-hour thyroid uptake, the 24-hour thyroid uptake, and the 0-to-24-hour urinary $^{131}$I excretion tests, carried out on 96 thyrotoxic, euthyroid, and hypothyroid patients. The same observer assessed the thyroid status of all patients, taking into account the clinical condition, basal metabolic rate, blood cholesterol level, response to treatment, and progress. In the series studied the first two tests showed an error of 5 to 7% in the diagnosis of thyrotoxicosis, the third test one of 10%, while the urinary excretion test was too inaccurate to be of value.

On the basis of these results it is suggested that the continuous thyroid uptake test is useful for distinguishing hyperthyroidism, particularly in clinics where large numbers of cases are seen and speed is an advantage. For other thyroid diseases, and also for the assessment of thyroid function in other diseases, the 15-minute continuous uptake test has no advantage over the 2-hour and the 24-hour uptake tests. *I. M. Rollo*

1486. **Treatment of Congenital Adrenal Hyperplasia with Concentrated Hydrocortisone Acetate**
N. N. LITMAN and G. N. DONNELL. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **20**, 862–868, June, 1960. 2 figs., 14 refs.

The administration of adrenal corticosteroids, either orally or parenterally, results in a decrease in the abnormal excretion of steroids in patients with congenital adrenal hyperplasia. Some patients, especially infants under 2 years of age, respond better to intramuscular than to oral therapy. There have been reports of successful results obtained by intramuscular injection of hydrocortisone acetate at intervals of 1 to 3 weeks, but the volume of the injected suspension has been 10 ml., an amount unsuitable for young children.

In this communication, from the Children's Medical Group (University of California), Los Angeles, the authors report the results in 10 cases of congenital adrenal hyperplasia in patients ranging in age from 27 months to 10 years, who received a concentrated suspension of hydrocortisone acetate injected intramuscularly every 2 weeks. The 2 weeks preceding the first injection of this preparation constituted the control period, during which time all the patients were receiving cortisone, or hydrocortisone, with or without deoxycorticosterone acetate. The initial dose of the concentrated suspension was 200 mg. in 1 ml., the further fortnightly doses being regulated according to the level of urinary 17-ketosteroid excretion. At the beginning and end of the period of study, which lasted for 6 to 9 months, estimations were made of: (1) bone age, judged by the radiographic appearances of the hand, wrist, and other bones; (2) the 24-hour urinary excretion of 17-ketosteroids and pregnanetriol.

By this method of administration adequate suppression of urinary 17-ketosteroid and pregnanetriol excretion was achieved in all cases, such excretion remaining suppressed between injections, while precocious bone maturation and linear growth were also arrested in every case. Unfortunately 3 of the children developed large sterile abscesses at the site of injection. This, it is thought, may have been due to inadvertent subcutaneous injection, but the authors regard the occurrence as a " major deterrent " to the use of this preparation.

*Kenneth Stone*

## PITUITARY GLAND

1487. **The Effect of Chlorpromazine on the Functions and Structure of the Anterior Lobe of the Hypophysis under Certain Experimental Conditions.** (Влияние аминазина на функции и структуру передней доли гипофиза при некоторых экспериментальных воздействиях)
B. V. ALEŠIN and L. A. US. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **6**, 32–45, May–June, 1960. 5 figs., 34 refs.

Current views on the hormonotrophic cells of the anterior lobe of the pituitary gland are that growth takes place and adrenocortical trophic hormones are produced in the acidophil cells, while the gonadotrophic and thyrotrophic hormones arise in the basophil cells. Furthermore, two separate main types of basophils have been distinguished, oval peripheral cells ($\delta$-basophils), which produce gonadotrophins, and large, predominantly centrally situated cells, " thyrotrophs ", which are the source of thyrotrophic hormone which the authors designate $\beta$-basophils.

While the difference in function of acidophils and of basophils is well established, some doubt as to the distinction between different types of basophils is raised by the results of the experiments here described on the action of chlorpromazine on the pituitary gland of white rats which were given subcutaneous injections of 2·5 mg. of chlorpromazine per 100 g. body weight in a 0·5% solution in physiological saline once daily for up to 7 days. The rats were then killed, the anterior lobes of the pituitary glands removed and sectioned, while from some of the tissue a suspension was made and 0·5 ml. injected into guinea-pigs (for estimation of thyrotrophic action) and 0·2 ml. into infant mice (for assay of the gonadotrophic activity), 6 such injections being given over a period of

4 days. The gonadotrophic as well as the thyrotrophic activity was definitely lowered in the hypophysis of rats receiving chlorpromazine, as compared with the controls. In sections of the anterior lobes, however, the number of basophil cells giving the glucoproteid reaction with MacManus's strain was much increased, as were the " thyrotrophs " giving the aldehyde–fuchsin reaction.

Two series of rats were then investigated, in one of which the thyrotrophic function had been intensified by a course of 6-methylthiouracil, and in the other gonadotrophic activity had been stimulated by castration. The rats receiving 6-methylthiouracil alone showed an increase in thyrotrophic activity and a slight rise in gonadotrophic activity; however, those treated with chlorpromazine as well showed a fall in gonadotrophic action, but paradoxically a much enhanced thyrotrophic effect. Chlorpromazine likewise depressed the gonadotrophic action in castrated rats (animals not given the drug showed increase of this function), but the thyrotrophic effect far exceeded that in normal controls. There was a great increase in $\delta$-basophil cells throughout the tissues of the anterior lobe, and many of these cells showed proliferation of the aldehyde–fuchsin staining granules usually regarded as typical of $\beta$-basophils, as well as the glucoproteid reaction. The authors consider that the thyrotrophs ($\beta$-basophils) should not be regarded as a specific type of cell, but rather as a temporary condition of these cells while undergoing intensified production of thyrotrophic hormone.

It is concluded that chlorpromazine acts by depressing the hypothalamus, and that impulses from this centre have a more profound effect upon the secretion of gonadotrophic hormone than upon that of thyrotrophic hormone; further, that it is not possible to suppress with chlorpromazine the latter hormone if the gland is stimulated (by castration or thyroid depression) to increased production. Although there is a fall in gonadotrophin output this is much less marked than in the case of normal animals treated with chlorpromazine. The basophil cells can act as gonadotrophs or as thyrotrophs according to the balance of impulses to the hypophysis from the hypothalamus. The characteristic cells found in castrated animals and those peculiar to thyroidectomy are almost absent in animals treated with chlorpromazine, but they are numerous in those not receiving the drug, suggesting that the appearance of these cells is due to nervous impulses from the hypothalamus.

*L. Firman-Edwards*

1488. **The Neurosection of the Hypothalamus and the Histochemistry of the Endocrine Glands in Itsenko–Cushing's Disease.** (Нейросекреция гипоталомуса и гистохимия эндокринных желез при болезни Иценко-Кушинга)

E. I. Tarakanov, V. F. Majorova, and T. A. Ščitkova. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **6**, 46–51, May–June, 1960. 5 figs., 40 refs.

The authors claim that Cushing's disease was first described by Itsenko in 1924 and only later by Cushing in 1932. The former associated it with lesions in the nerve-cells of the hypothalamus, including degeneration of the supra-optic and paraventricular nuclei. After a brief description of the course of the nerve-tracts from these nuclei to the posterior pituitary lobe, the authors show how the secretion passes along the axons of the cells of the nuclei and is deposited in large agglomerations of granules of varying size in the neighbourhood of the terminals of the axons and in the corpuscles of Hering. This is, however, not the only route, for many of the granules pass into the capillaries and also into the cells of the ependyma of the third ventricle and so into the cerebrospinal fluid.

In 2 patients with the disease who died, one from hypertensive heart failure and one from pneumonia, the structures of the central nervous system and endocrine glands were examined histochemically post mortem. It was found that the nerve cells of the supra-optic, paraventricular, and tuberal ganglia were markedly degenerated and pale, their contours being pale and indistinct, with small and ectopic nuclei, the tigroid dispersed, and the cytoplasm vacuolated. Neurosecretin was clumped in the centre of the cells, but was not found in the dendrites or axons. In the posterior pituitary lobes there was almost complete absence of neurosecretin and very few Hering's corpuscles were present. The anterior lobe in both cases contained a basophil adenoma composed of deeply staining cells full of ribonucleinic acid and glucoproteids, and encapsulated by connective tissue. Outside the adenoma the cells of the adenohypophysis were predominantly acidophil; chromophobe cells were scarce. In the adrenal glands there was hyperplasia and hypertrophy of the cortex, and in places " micro-adenomata " of this tissue invaded the medulla. The cells were full of lipoids and ketosteroids. In the external part of the fascicular zone, however, these were fewer, and in all zones there were patches of cells almost devoid of lipoids; but these cells stained deeply with Ashbell–Zeligman stain for ketosteroids. Glucoproteids were abundant in the reticular zone, less so in the others, though the glomerular zone stained more deeply for these than is usual in normal glands. In the thyroid gland the alveoli were of varying sizes, the epithelium flat or cubical, and the colloid dense and in some alveoli vacuolated. The nuclei of epithelial cells were in some places desquamated, in others pyknotic. The cells were pale and stained hardly at all for glucoproteids or for ribonucleinic acid.

In the pancreas the islet tissue was hypertrophied, especially the $\beta$-cells, in which glucoproteids were abundant. Many cells had twin nuclei. The $\alpha$-cells stained less intensely for glucoproteids. There was no change in the content of ribonucleinic acid. In regard to the gonads, the ovaries in one case and the testes in the other were atrophied, with increase in interstitial connective tissue. The thymus gland showed fatty degeneration with lymphoid infiltration. Hassall's corpuscles were degenerate, the central parts staining more deeply for glucoproteids than the periphery. There was no staining for ribonucleinic acid in these cells. The authors regard the disturbance of hypothalamic action as the primary cause of the disease, and the changes in the adenohypophysis as secondary, including the formation of adenomata. Changes in the other endocrine glands

follow as a matter of course. The hypertrophy of the islets of the pancreas is a response to the increased production of steroid hormones. *L. Firman-Edwards*

## DIABETES MELLITUS

1489. ***Ortho*-Cresotinate and Diabetes Mellitus**
T. D. LIGHTBODY and J. REID. *British Medical Journal* [*Brit. med. J.*] **1**, 1704–1707, June 4, 1960. 6 refs.

The value of *ortho*-cresotinate, a compound related to aspirin, in diabetes mellitus was studied in 9 patients at the Western Infirmary, Glasgow. Of the 9 patients 6 had been treated previously by dietary restriction only for periods of one month to 2 years and 3 had been treated in addition with insulin zinc suspension (I.Z.S.) in a dosage of 28 to 88 units daily. The drug was given as acetyl-*ortho*-cresotinate orally in a dosage of 1 to 1·3 g. 4-hourly to 8 patients and as a solution of sodium *ortho*-cresotinate to one patient. The dosage was controlled by frequent estimation of the serum *ortho*-cresotinate level, the aim being to maintain a level of 30 to 35 mg. per 100 ml. The course lasted 2 weeks.

At the end of a control period of dietary restriction only 3 of the 6 patients were free from diabetic symptoms, but at the end of the course of *ortho*-cresotinate all 6 were symptom-free. In this group administration of *ortho*-cresotinate resulted in a significant fall in the fasting blood sugar level (in 5 of the 6 patients to within normal limits), a significant reduction in glycosuria, and a quantitative but not qualitative reduction in the oral glucose tolerance level. Of the 3 patients treated by dietary restriction and insulin, *ortho*-cresotinate replaced a daily dose of 28 units I.Z.S. in one and reduced considerably the daily dose of I.Z.S. in 2. Side-effects with *ortho*-cresotinate, which included anorexia, headache, and nausea and vomiting, were temporary and were in general related to the serum *ortho*-cresotinate level. Deafness and tinnitus were not observed. It is concluded that *ortho*-cresotinate can lower the blood sugar level in the milder diabetic without the deafness and tinnitus produced by the related compound, aspirin.
*Gerald Sandler*

1490. **Maternal Diabetes. Changes in the Hearing Organ of the Embryo: Additional Observation**
G. KELEMEN. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **71**, 921–925, June, 1960.

Although it has been known for at least a century that there was some association between diabetes and damage to hearing and vestibular function, the main interest in the past has been centred on the danger of middle-ear suppuration in diabetic patients. In recent times this has been controlled by the use of insulin, sulphonamides, and antibiotics. There remains, however, the problem of the effects of diabetes on the inner ear, and particularly those of maternal diabetes on the ear of the foetus. The present author reports the changes found in the inner ear in 2 embryos of women with diabetes whose pregnancies were interrupted on medical grounds by hysterotomy at the fourth and fifth months respectively. (These 2 cases, one of which was previously described by the author (*A.M.A. Arch. Otolaryng.*, 1955, **62**, 357) seem to have been the first embryos of diabetic patients examined histologically.) In each case the outstanding abnormality was a tendency to rupture of the vessels and haemorrhage, with resultant damage to the sensory end-organs of the inner ear, with destruction of cupulae.

[These findings suggest that more attention should be paid to the occurrence of hereditary deafness in the children of diabetic mothers, since the earlier such a condition is noted, the better will be the chance of suitable training for the child.] *F. W. Watkyn-Thomas*

1491. **The Prognosis in Diabetes with Onset before Age Two.** [In English]
O. IMERSLUND. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **49**, 243–248, May, 1960. 7 refs.

Of 3,847 juvenile diabetics treated at the Joslin Clinic, Boston, between January, 1922, and December, 1956, the diabetes had started before the age of 2 years in 118. A follow-up study, partly by postal enquiry, showed that by the end of 1956 20 were dead and 25 could not be traced. The cause of death was not known in 2 cases, 7 patients died from infections (but none since 1954), 6 from coma (but none since 1948), one from hypoglycaemia, one from suicide, and 3 from degenerative vascular complications; the ages of these last ranged from 26 to 34 years and the average duration of the diabetes was 29 years. Retinitis was present in 2 of the 9 patients examined before the age of 10, while the incidence of retinopathy varied from 10% in those in whom the disease had lasted 10 to 14 years to 100% in those in whom duration was 30 years. The youngest patient to suffer blindness from retinitis proliferans was aged 20, having been diabetic for 19 years, and the youngest with arterial calcification was aged 18, but only 2 of the patients examined after the disease had been present for more than 20 years were free from this complication. Significant proteinuria was found in 4·3% of those with a disease duration of 15 to 19 years, the incidence rising to 50% after a duration of 30 to 34 years.

The course of degenerative vascular complications varied widely; in one patient who had retinopathy at age 14 the condition showed little progression in the next 13 years, whereas another who after 24 years of diabetes died from the Kimmelstiel–Wilson syndrome showed no significant proteinuria at examination 2 years earlier. The presence of complications could not easily be related to the quality of diabetic control since the patients were not all under the close supervision of the clinic, but it is noted that the patient with the earliest onset of nephropathy and blindness had taken a free diet and had been under poor control, whereas the one patient without complications after 25 years of the disease was himself a doctor and the son of a doctor and the diabetes had been under good control. Pointing out that in this study the incidence of degenerative vascular complications in patients with diabetes of less than 30 years' duration was lower than in other studies of juvenile diabetes with a more widespread age of onset, the author suggests that possibly some additional pathogenic factor develops after puberty. *F. P. Hudson*

# Physical Medicine

1492. **Motor Nerve Conduction Velocity Studies in Poliomyelitis**

E. W. JOHNSON, J. D. GUYTON, and K. J. OLSEN. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **41**, 185–190, May, 1960. 5 figs., 8 refs.

At the Children's Hospital, Columbus, Ohio, motor-nerve conduction velocity was studied in 100 patients with acute poliomyelitis of at least 3 weeks' duration. The median, ulnar, peroneal, or posterior tibial nerve was tested, a square wave impulse of 0·2 to 0·4 milliseconds and an intensity of 60 to 90 volts being employed. Both coaxial and monopolar needle electrodes were used in conjunction with the electromyograph. [Full details of the apparatus are not given.] In most of the patients the temperature of the tissue in the vicinity of the nerve in the middle of its course was recorded.

A total of 162 motor-nerve conduction velocity measurements were obtained in 98 of the patients. In 92 patients with laboratory evidence of poliomyelitis the conduction velocities ranged from 40 to 69 metres per second (m./sec.) and were considered to be within the normal range. The mean values for these patients were 50 m./sec. for the peroneal nerve, 54·4 m./sec. for the ulnar nerve, 53·2 m./sec. for the median, and 49·0 m./sec. for the posterior tibial nerve. In 6 patients conduction velocities were reduced by at least 40%, the values ranging from 1·5 to 32 m./sec.; these patients had no laboratory evidence of poliomyelitis and the subsequent course of the illness suggested a diagnosis of acute infectious polyneuritis. Electromyographic examination in 99 patients revealed evidence of lower motor neurone disease. The average of 39 temperature measurements in the arm was 35° C., while of 67 measurements in the leg the average was 34·2° C.

The authors discuss previous work and stress that motor-nerve conduction velocity in patients with poliomyelitis is normal. Infants over 18 months old have "low-adult values" and in infants under this age conduction is reduced. Temperature appears to influence motor conduction velocity; some workers have reported a 5% reduction per degree centigrade. If motor conduction velocities are reduced 2 to 3 weeks after the acute onset of paralysis polyneuritis should be diagnosed.

*J. B. Millard*

1493. **Electromyogram in Neuromuscular Re-education**

A. A. MARINACCI and M. HORANDE. *Bulletin of the Los Angeles Neurological Society* [*Bull. Los Angeles neurol. Soc.*] **25**, 57–71, June, 1960. 6 refs.

The authors, using electromyography as an aid to neuromuscular re-education, have found that by allowing the patient actually to hear the noise produced by his own muscular contractions he is able to re-educate himself. There are two specific groups of subjects in whom audioneuromuscular re-education has been found to be of considerable value: (1) the large group of patients in whom a considerable amount of latent function is detected; and (2) those in whom latent function is minimal.

[This is not a well-written paper and many of the statements are difficult to fit in with orthodox views on neurophysiology. It would seem, however, that this method of re-education has possibilities.]

*N. S. Alcock*

1494. **A Method for Increasing the Depth Heating Effect of Infrared Radiation**

R. HARRIS and S. K. SARKAR. *Annals of Physical Medicine* [*Ann. phys. Med.*] **5**, 252–257, Aug., 1960. 1 fig., 5 refs.

A modified technique of applying a radiant heat source to skin surfaces is described in this paper from Devonshire Royal Hospital, Buxton. It consists in combining the conventional method of applying radiant heat with the use of an electric fan, which moves air at room temperature over the heated part. The results obtained with this technique showed that the source of heat could be tolerated closer to the skin surface, and that a significantly greater heating of deeper tissues was achieved, down to one inch (2·5 cm.) below the surface.

*Allan St. J. Dixon*

1495. **Changes in Blood Flow, Oxygen Uptake and Tissue Temperatures Produced by Therapeutic Physical Agents. I. Effect of Ultrasound**

D. I. ABRAMSON, C. BURNETT, Y. BELL, S. TUCK JR., H. REJAL, and C. J. FLEISCHER. *American Journal of Physical Medicine* [*Amer. J. Phys. Med.*] **39**, 51–62, April, 1960. 2 figs., 16 refs.

The effect of ultrasonic irradiation on the blood flow, oxygen uptake, and tissue temperature in the forearm of 16 male subjects aged 21 to 39 was studied at the University of Illinois College of Medicine, Chicago. The irradiation was applied by means of two stationary heads each 10 sq. cm. in area incorporated in the plethysmograph, one being placed over the brachioradialis muscle and the other more distal and held at least 1 cm. from the skin. A pulsed ultrasonic generator with a frequency of 1 megacycle and an output of up to 30 watts was connected to each head, the dose being regulated to avoid discomfort. Blood flow was measured by means of a venous occlusion plethysmograph, the water temperature being kept at 34°C. The temperature of the proximal part of the forearm was measured by thermocouples on the skin, in the subcutaneous tissue, and the brachioradialis muscle. Venous blood was collected from the antecubital vein for oxygen content analysis. In each experiment the apparatus was first connected and 5 or 6 control measurements taken after 90 minutes. Ultrasonic irradiation was then applied for 20 minutes and measurements taken at intervals of 2 to 3 minutes until control levels were reached.

The results, which are tabulated for each individual, showed that in all subjects there was an increase in blood flow, the average being 100%, and this was maintained for 10 to 15 minutes after irradiation was stopped. The total excess oxygen uptake was apparently increased by 2·0 ml. per 100 c.cm. of limb volume. The mean maximum increases in temperature were: in the skin 0·9°C., in the subcutaneous tissue 1·4°C., and in muscle 0·9°C. The increases in blood flow, oxygen uptake, and temperature coincided in time, but there was no correlation between the amount of increase in these factors.

The authors discuss their results and those of similar reported studies. They conclude that " the increase in oxygen uptake which accompanies the augmentation in blood flow and rise in tissue temperatures precludes the use of ultrasound as therapy when an impaired local arterial circulation exists ". *J. B. Millard*

1496. **Changes in Blood Flow, Oxygen Uptake and Tissue Temperatures Produced by Therapeutic Physical Agents. II. Effect of Short-wave Diathermy**

D. I. Abramson, Y. Bell, H. Rejal, S. Tuck Jr., C. Burnett, and C. J. Fleischer. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] **39**, 87–95, June, 1960. 2 figs., 16 refs.

In an earlier paper (*Arch. phys. Med.*, 1957, **38**, 369; *Abstr. Wld Med.*, 1957, **22**, 469) the effect of short-wave diathermy on peripheral blood flow in the forearm was reported. In this further study carried out at the University of Illinois College of Medicine, Chicago, the investigation was extended to cover concomitant changes in tissue temperature and oxygen uptake. In 14 healthy male subjects short-wave diathermy was applied for 30 minutes with one electrode on the wrist and the other over the shoulder. Blood flow in the forearm was measured by a water-filled plethysmograph, tissue temperature changes were recorded by means of thermocouples in polyvinyl tubing placed in the upper forearm muscles, while for calculation of oxygen uptake venous blood samples were taken via a catheter inserted into a deep vein in the antecubital space. Readings were taken at intervals before, during, and after each experiment, and the results are presented in detailed tables.

Blood flow gradually increased by an average of about 100%, with a peak at 26 minutes, and the increase persisted for half an hour after heating ceased. Oxygen uptake showed similar increases, but changes in oxygen arterio-venous difference were small. Tissue temperature rose gradually, the average rise in the skin being 1·3° C., in subcutaneous tissue 1·5° C., and in muscle 1·9° C.; in all three tissues the rise reached its peak at approximately 26 minutes. These results and those of reported studies are discussed. *J. B. Millard*

1497. **Treatment of Pain in Preaxial Border of Upper Limb**

T. Wareham and R. Farrow. *Lancet* [*Lancet*] **2**, 336–338, Aug. 13, 1960. 6 figs.

At St. Bartholomew's Hospital, London, neck traction in flexion was employed in the treatment of 100 patients with pain in the preaxial border of the upper limb. For application of traction the head was supported on pillows, a small electric pad was placed behind the neck and upper thoracic region in order to aid relaxation, and a Niels Larsen type of halter was applied to the neck and attached to a " spreader ". After the face had been turned towards the painful limb, a pulley circuit with a weight of 14 to 21 lb. (6·4 to 9·6 kg.) was attached to the apparatus. The method is illustrated. Usually the pain receded about half a minute after the correct angle of traction had been obtained. With an average of 18 treatments every patient eventually became free from pain. The authors also point out that manual traction, although time-consuming, is equally effective and is " ideal " for use in the patient's home. A correct sleeping posture is of importance, and the patient should be warned not to sleep prone with the head turned sideways. In severe cases a sponge rubber collar may be employed with advantage.

In discussion the authors admit that the treatment is empirical. In fact, radiological examination of the cervical spine at no time revealed any significant abnormality apart from the degenerative changes associated with increasing age. It is emphasized, however, that neck traction in the neutral or extended position is a useless procedure. Without attempting to dogmatize as to the mechanism by which the pain is relieved the authors are content to recall the fact that in middle age the neurocentral joints of Luschka may show hypertrophic degenerative changes. These changes are most often to be found in the joints which lie in contact with the 5th and 6th cervical nerves, and the most common sites of pain in the upper limb are found in the 5th and 6th cervical dermatomes. *A. Garland*

1498. **Physical Factors Concerned with the Stiffness of Normal and Diseased Joints**

V. Wright and R. J. Johns. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **106**, 215–231, April, 1960. 23 figs., 5 refs.

A study of the physical factors concerned with stiffness of normal and diseased joints is reported from the Johns Hopkins University School of Medicine and Hospital, Baltimore. The various components of joint stiffness (elasticity, viscosity, inertia, plasticity, and friction) were measured quantitatively, a device in which a heavy pendulum rotated a shaft and lever which was firmly attached to the index finger being used; the axis of rotation was carefully adjusted to coincide with that of the second metacarpo-phalangeal joint. With the pendulum at rest the finger was at the mid-point of normal joint motion, and the maximum amplitude was 30 degrees each side of this joint. Gauges attached to the shaft measured torque, amplitude, and rotational velocity, the results being displayed on a dual-beam cathode-ray tube so that torque was shown against amplitude and velocity.

In a study of 97 non-arthritic subjects it was found that the main components of joint stiffness were the elastic and plastic components and that viscous stiffness was about one-tenth and inertial stiffness about one-hundredth that of elastic stiffness. Frictional stiffness could

not be demonstrated. It was also found that elastic stiffness was 3 to 4 times greater in the oldest subject (66 years) than in the youngest (4 years). It was increased by cooling the joint and decreased (by about 20%) by heating to 44° C. Venous occlusion caused a gradual increase in stiffness to a maximum after 30 minutes, but there was a return to normal immediately occlusion ceased. Arterial occlusion resulted in a marked increase in stiffness after 25 minutes, but again this disappeared rapidly when occlusion ceased. No muscular activity could be detected electromyographically during these experiments.

Patients with rheumatoid arthritis showed increased elastic stiffness; in one patient, treatment with steroids reduced the stiffness almost to normal levels. Viscous stiffness was rather greater than in healthy subjects, but was still relatively an unimportant factor. Frictional stiffness was detected in a case of rheumatoid arthritis with gross joint changes and in a case of gout, but it was small in relation to the elastic stiffness present. A patient with systemic sclerosis had increased elastic stiffness while 2 with Ehlers–Danlos syndrome and 7 with Marfan's syndrome had decreased elastic stiffness.

*B. E. W. Mace*

1499. **Back Pain and Hyperaesthesia**

J. R. GLOVER. *Lancet* [*Lancet*] **1**, 1165–1169, May 28, 1960. 4 figs., 11 refs.

A syndrome of back pain which has been commonly observed in patients in an industrial practice is described. The features of this back pain, which may occur anywhere from the occiput to the coccyx, are an area of hyperaesthesia with a localized tender spot and a dull ache and pain elicited by trunk movement. Between 1953 and 1958 a total of 239 patients suffering from this syndrome came to the author's notice and 100 have been studied in detail. The lower segments of the spine were more frequently affected than the upper. Of the 100 patients, 86 showed between them 132 examples of the complete syndrome. Manipulation was carried out except where there was involvement of the cervical region, with a successful outcome in 86 out of 97 instances.

The author points out, however, that the condition may disappear spontaneously. He considers that this syndrome is a disturbance of mesodermal structures. While the exact cause is not known it is suggested that the structure at fault is connected with the apophysial synovial vertebral joints and could possibly be a ligament or the synovial membrane.

*W. Tegner*

1500. **Short-leg Syndrome**

P. J. R. NICHOLS. *British Medical Journal* [*Brit. med. J.*] **1**, 1863–1865, June 18, 1960. 4 figs., 12 refs.

From a Royal Air Force rehabilitation unit comes this report on the association between difference in leg lengths and low backache. Analysis of previous studies on this subject led the author to conclude that only a difference in leg length of 11 mm. or more was significantly correlated with clinical symptoms. In the present study a difference in the measurements from the anterior superior iliac spine to the tip of the medial malleolus in the two legs of ½ inch (12·5 mm.) or more was accepted as the criterion for the clinical diagnosis of " short leg ".

The leg lengths of all patients admitted to the rehabilitation unit during one year were recorded. By the above criterion, of 1,007 patients with conditions other than backache, and with no history of it, 72 (7%) had a short leg. Of 180 patients with low backache 39 (22%) had short leg; in only 7 of these was the backache not attributable to other possible causes than short leg, such as postural defects or prolapsed intervertebral disk. These 7 patients were all relieved of pain by raising the height of the shoe. Backache due to short leg is usually gradual in onset, and starts in late adolescence or early adult life. It may be the result of shortening of the leg after a fracture, though in such case the onset of symptoms may be delayed for many years. There appears to be no other way of assessing the part played by short leg in the causation of low backache than by trying the effect of a shoe-raise. Six illustrative case histories are briefly detailed.

*Kenneth Stone*

1501. **Results of Rehabilitation and Resettlement in Rheumatoid Arthritis**

R. HARRIS. *Annals of Physical Medicine* [*Ann. phys. Med.*] **5**, 194–202, May, 1960. 6 refs.

During the 5-year period 1953–8, of the 1,928 patients admitted for treatment to the rehabilitation unit of the Devonshire Royal Hospital, Buxton, Derbyshire, nearly half (988) had rheumatoid arthritis. There was a preponderance of females in the ratio of 1·9:1, as compared with 1·4:1 for all admissions, and 59% of the patients were in the age group 40 to 60 years. Although the disease was chronic in the majority of these patients severe disability was of relatively recent origin.

At the time of admission to the unit 55% of the patients showed considerable disablement, but on discharge only 25% did so. The corresponding figures for those who were regarded as being " fit for any work " were 14 and 51% respectively. In 69% of cases the duration of in-patient treatment at the unit was less than 3 months. When it was considered that a change of occupation was indicated the cases were discussed at a resettlement clinic attended by, among others, a disablement resettlement officer, an almoner, and a member of the medical staff with special experience in industrial medicine. Follow-up observations were maintained for 2 to 3 years after discharge, and showed that more than half the subjects had remained in steady employment. Resettlement as skilled clerical workers was achieved by most of the women who had been so employed before their illness. On the other hand, male workers employed in heavy industry usually returned to less skilled employment; for instance, one former worker at the coal face became a surface-haulage hand. Only 20% of the men were placed in skilled jobs, as compared with 52% initially in such jobs. Nevertheless, the results compare favourably with those obtained by other investigators, for almost all those who had been placed at work within 3 months of discharge from hospital were still in employment 2 to 3 years later.

*A. Garland*

# Neurology and Neurosurgery

1502. **Suppression by Anticonvulsants of Focal Electrical Seizures in the Neocortex**
E. F. Vastola and A. Rosen. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **12**, 327–332, May, 1960. 6 figs., 4 refs.

In the experimental studies here reported from the State University of New York College of Medicine, Brooklyn, bipolar recording electrodes were inserted into the upper layers of the visual cortex of 23 cats with incomplete transection of the brain stem. Stimulating electrodes were also inserted into the upper layers of the visual cortex and seizures were elicited by means of square wave pulses of 1 millisecond duration at 70 per second for 10 seconds, delivered by a Grass stimulator. The seizures, which were provoked regularly at intervals of 5 or 10 minutes and lasted from 5 to 120 seconds, could be elicited without any change in their characteristics for periods ranging from 2 to 4 hours. Mainly they remained focal, but occasionally they were generalized, as indicated by clonic movements of the limbs.

The administration of 5 mg. of sodium phenobarbitone per kg. body weight led to a marked decrease in the amplitude and duration of the seizure activity. " Dilantin " (phenytoin sodium), 4 to 8 mg. per kg., and " nembutal " (pentobarbitone sodium), 4 to 5·5 mg. per kg., each had similar effects, but " tridione " (troxidone), 14 to 28 mg. per kg., had no effect. The authors suggest that the technique may help in assessing the value of new anticonvulsant drugs. *L. G. Kiloh*

1503. **Treatment of the Carpal-tunnel Syndrome**
R. S. Crow. *British Medical Journal* [*Brit. med. J.*] **1**, 1611–1615, May 28, 1960. 28 refs.

The author, writing from the Bristol Royal Infirmary, discusses the results in 81 patients suffering from the carpal tunnel syndrome, of whom 19 received no active treatment, 36 were treated by immobilization (bilateral in 18 cases) by means of a close-fitting anterior plaster-of-Paris splint worn at night, 22 by injection of hydrocortisone into the carpal tunnel, and 31 (many of whom had not responded to the other forms of treatment) by operative division of the flexor retinaculum. He concludes (1) that surgical treatment offers almost certain and permanent relief; (2) local injection of hydrocortisone is useful as a diagnostic measure, as a means of rapid alleviation of severe symptoms, and as the sole treatment in a limited number of cases; (3) immobilization gives a satisfactory result in about 40% of cases, whatever their severity or duration. Of the 19 patients who were not given any active local treatment 13 remitted spontaneously and remained free of symptoms for follow-up periods varying from one to 5 years; of the other 6 one patient, an acromegalic, improved after radiotherapy to the pituitary gland, but in the other 5 symptoms of varying severity persisted. *J. W. Aldren Turner*

1504. **Acroparaesthesiae and Acromegaly**
A. W. Johnston. *British Medical Journal* [*Brit. med. J.*] **1**, 1616–1618, May 28, 1960. 1 fig., 20 refs.

Only 9 cases of acromegaly with acroparaesthesiae due to median-nerve compression in the carpal tunnel appear to have been reported in the literature. In this paper from Whittington and University College Hospitals, London, 5 further cases are described, together with the necropsy findings in another case of acromegaly in which there was no history of pain or of paraesthesia in the hands. In this last case the anterior carpal ligaments were both thickened, with compression of the median nerves. The sex incidence of the carpal-tunnel syndrome in acromegalics is said to be equal, unlike the marked predominance of females with acroparaesthesiae without acromegaly. The author suggests that the " variation in symptoms of acroparaesthesiae is due to a soft-tissue component acting in the confined space of the carpal tunnel and that this effect is exacerbated by the local overgrowth of the structures forming the tunnel in acromegaly ". *J. W. Aldren Turner*

## BRAIN AND MENINGES

1505. **Visual-constructive Disabilities Associated with Lesions of the Left Cerebral Hemisphere**
J. McFie and O. L. Zangwill. *Brain* [*Brain*] **83**, 243–260, June, 1960. 4 figs., 27 refs.

At the National Hospital, Queen Square, London, the authors have studied a group of 8 patients in whom there was a lesion of the left cerebral hemisphere accompanied by a prominent degree of visual-constructive impairment. In contrast to patients with small right-sided lesions the disability in this group was rarely associated with unilateral neglect, apraxia for dressing, or failure in tests involving spatial analysis. The disability was frequently associated with right–left disorientation and intellectual impairment. In all 8 cases the lesion was in the posterior parietal region and the authors make a plea for fuller analysis of disability in patients with adequately localized lesions in the future. *Hugh Garland*

1506. **Constructional Apraxia Associated with Unilateral Cerebral Lesions—Left and Right Sided Cases Compared**
M. Piercy, H. Hécaen, and J. de Ajuriaguerra. *Brain* [*Brain*] **83**, 225–242, June, 1960. 4 figs., 28 refs.

The incidence of constructional apraxia was studied in over 3,000 patients seen at the neurosurgical service of the Hôpital Sainte-Anne, Paris, between 1947 and 1959. Of these patients 80 had constructional apraxia, but 13 had bilateral cerebral lesions. Of the 67 with a unilateral lesion this was right-sided in 42 and left-sided in 25. In all cases the lesions were in the temporal,

parietal, or occipital lobe, or in more than one of these, and there was a wide variety of pathological disturbances. It was found that constructional apraxia was more frequent and more severe following damage to the right hemisphere and that the location of the lesion responsible tended to be more restricted in cases of right hemisphere lesion. The difference between the two groups both as regards severity and frequency of the disability could not be accounted for by the masking effect of weakness, dysphasia, or unilateral imperception, nor could the qualitative differences be attributable to severity alone. It is concluded that the right cerebral hemisphere in right-handed persons has a special and non-subordinate role in the cognitive functions involved in normal constructional performance. *Hugh Garland*

1507. **Apraxia of Gait: a Clinico-physiological Study**
J. S. MEYER and D. W. BARRON. *Brain* [*Brain*] **83**, 261–284, June, 1960. 7 figs., 45 refs.

Writing from Wayne State University College of Medicine, Detroit, the authors define apraxia of gait as a loss of ability to use the lower limbs in the act of walking which cannot be accounted for by sensory impairment or motor weakness. A comprehensive review of the literature has revealed considerable disagreement concerning the nature of disorders of gait in cerebral disease. The term " frontal ataxia " has been frequently used to describe disturbances of gait due to various combinations of the following possible mechanisms. (1) Large expanding lesions of the frontal lobe may produce massive displacement of intracranial structures with cerebellomedullary compression and clinical signs of cerebellar dysfunction and ataxia. (2) Space-occupying lesions of the frontal lobes with brain displacement may also cause compression of the 8th cranial nerve and produce vertigo and ataxia. (3) Frontal lobe lesions which do not displace intracranial structures may produce apraxia of gait in the abscence of cerebellar signs.

Apraxia of gait may result from any of the following lesions: a tumour or abscess in the frontal lobes, infarction of the frontal lobes due to atherosclerosis of the anterior cerebral arteries, cerebral haemorrhage, presenile and senile dementia, and paretic neurosyphilis. The authors analyse the clinical signs that differentiate frontal lobe apraxia from cerebellar ataxia and describe in detail 7 cases exhibiting apraxia of gait.

*A. G. Freeman*

1508. **Anticoagulant Therapy in Acute Cerebrovascular Accidents: a Controlled Trial**
J. MARSHALL and D. A. SHAW. *Lancet* [*Lancet*] **1**, 995–998, May 7, 1960. 1 fig., 16 refs.

The object of this investigation, which was carried out at the National Hospital, Queen Square, London, was to determine whether a specific medical treatment aimed at the pathological lesion was effective in patients suffering from a " stroke ". The authors point out that vasodilator drugs, corticosteroid therapy, and stellate-ganglion block have all been tried but none has been proved to be of value when subjected to controlled clinical trial. Patients suffering from acute cerebrovascular accidents were given 3 intravenous injections of heparin at 6-hourly intervals and phenindione in a dosage which would maintain the prothrombin time (determined by the Quick one-stage method) at two to three times the control value. All the patients were subjected to angiography of the appropriate cerebral vessel (carotid or vertebral). Patients over 70 years of age and those with embolism, severe hypertensive retinopathy, left ventricular failure, evidence of peptic ulceration, bleeding disease, or severe liver or renal disease were excluded from the trial. The patients were divided at random, into two groups—one group of 26 receiving anticoagulant treatment and the other group of 25 serving as controls. Anticoagulant therapy was given for 21 days and then gradually withdrawn. Since it was desirable that the trial should be discontinued at once if it appeared that the treatment was having no beneficial effect, the method of sequential analysis was used. Survival or failure to survive for 6 weeks from the start of treatment was the criterion on which the results were based. The analysis did not reveal any difference in favour of anticoagulant therapy and the trial was accordingly stopped. Of the 26 patients given anticoagulants 20 survived to 6 weeks and of the 25 controls 22 survived to 6 weeks. Necropsy, which was performed in 8 of the 9 fatal cases, showed that in the group given anticoagulants there were 3 cases of cerebral haemorrhage which was not diagnosed during life, although lumbar puncture and cerebral angiography had been carried out.

It is concluded that " anticoagulants, when used according to the criteria of selection and management of the trial, are not of value ". *G. S. Crockett*

1509. **Elipten: a Clinical Evaluation of a New Anticonvulsant. Preliminary Report**
K. I. PEARCE. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **82**, 953–959, May 7, 1960. 3 figs.

Previous workers have found that the anticonvulsant properties of the hypnotic glutethimide " doriden " could not be fully utilized because of the marked sedative action of the drug. In this paper from Union Hospital, Moose Jaw, Saskatchewan, a clinical trial is reported of " elipten ", a related glutethimide derivative, which appears to be more promising for practical use as an anticonvulsant. The drug was given to 12 male patients in a mental hospital who had suffered from grand mal (or mixed grand mal, petit mal, and psychomotor seizures) for many years and were poorly controlled by standard anticonvulsants. The patients acted as their own controls, behaviour and frequency of seizures during previous standard anticonvulsant treatment being compared with these factors during administration of elipten and subsequently during treatment with doriden. In half the cases elipten was given alone in an average daily dosage of 1,500 mg., but in the remainder it was combined with other anticonvulsants to achieve optimum control. Elipten was given for 2 to 12 months followed by doriden for 1 to 5 months. In 10 patients behaviour much improved during elipten therapy and in one of them seizures were completely controlled. In 3 cases the complete control obtained with previous medication

was maintained during treatment with elipten and when doriden was substituted. In 9 cases the electroencephalogram (EEG) improved during the trial; in the remaining 3 there was improvement in behaviour during elipten therapy but no change in the EEG. No toxic or side-effects were observed. It is concluded that elipten may permit a considerable reduction in the dosage of standard anticonvulsant drugs in those cases of epilepsy in which control is difficult and may bring about improvement in behaviour of disturbed epileptics in hospital.

*J. B. Stanton*

1510. **Introduction of Caffeine in High Dosage into the Treatment of Epilepsy.** (Introduction de la caféine à fortes doses dans le traitement de l'épilepsie)
J. P. JUNOD and F. MARTIN. *Psychiatria et neurologia [Psychiat. et Neurol. (Basel)]* **139**, 205–220, April [received June], 1960. 16 refs.

This paper describes the results of adding pure caffeine in a dosage of 100 to 400 mg. daily to the routine treatment with anticonvulsant drugs of 133 patients at the Institution for Epileptics, Lavigny, Switzerland. Most of the patients were insufficiently stabilized while taking methoin, phenytoin sodium, and phenobarbitone. There was improvement in 85 of these patients in regard to the frequency of attacks, changes in bearing, and modification of intellectual efficiency; no change was noted in 20 patients, and 28 patients were definitely worse, with increased frequency of attacks. In 8 of this last group a toxic syndrome characterized by diurnal somnolence, nocturnal agitation, cerebellar ataxia, character disorder, and even violence developed. Patients with organic epilepsy of focal or diffuse origin responded better than did those with idiopathic epilepsy; benefit was also obtained by those in whom the electroencephalogram was aggravated by hyperventilation. *I. Ansell*

## SPINAL CORD

1511. **Intervertebral Disk Protrusions in Childhood and Adolescence**
J. E. A. O'CONNELL. *British Journal of Surgery [Brit. J. Surg.]* **47**, 611–616, May, 1960. 1 fig., 10 refs.

Since it has been suggested that the clinical picture of intervertebral-disk protrusion in childhood differs from that in adolescence the author analysed a series of 38 cases of lumbar-disk protrusion out of a total of 1,222 operated on at St. Bartholomew's Hospital, London, between 1938 and 1958. In all 38 patients symptoms developed at or before the age of 17, and the features in this group are compared with those in a previously reported consecutive series of 500 patients unselected for age (*J. Bone Jt Surg.*, 1951, **33B**, 8; *Abstr. Wld Surg.*, 1951, **10**, 141).

There was an increased proportion of females in the younger-age series compared with the unselected series. This was thought to be due to the fact that in the female the period of rapid increase in weight (11 to 15 years) and height (9 to 14) occurs earlier than in the male; it is suggested that stress during this period may have some aetiological significance. In the younger group as in the unselected the outstanding symptom was pain, involving in most instances the low back and posterior crural areas together. Symptoms other than pain and paraesthesiae were uncommon; none of the younger patients had severe subjective disability from neurological deficit compared with 4% of the unselected series. Young patients tended to have more persistent pain with fewer remissions, but complained less. Tension signs, such as limitation of straight-leg raising, were more severe in the young, but neurological abnormalities were less frequent and less severe. Radiological changes were more common in the unselected series than in the children, but the operative findings in both were comparable. The results of operation were slightly better in the children, but the incidence of recurrence and re-operation (6%) was higher than in the larger series (2·3%).

It is suggested that the differences observed in the clinical picture may be due to the fact that in the more mobile spine of youth there are more severe deformity and fixation designed to protect the nerve roots from damage, and that these lead to a reduction in the neurological signs. *Brodie Hughes*

1512. **Lumbar Disc Protrusions in Pregnancy**
J. E. A. O'CONNELL. *Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Neurosurg. Psychiat.]* **23**, 138–141, May [received July], 1960. 5 refs.

At St. Bartholomew's Hospital, London, analysis of the records of 347 consecutive female patients with surgically proven intervertebral-disk protrusion revealed that in 179 (51%) pregnancy had taken place. In 70 (39·1%) of these, symptoms of lumbar-disk protrusion developed during pregnancy (42), during labour (8), or during the puerperium (20). A lower-limb paresis of severe or moderate degree occurred in 12 of the 70 patients and involved the ankle and occasionally the knee- and hip-joints, the paresis developing in the early puerperium in 3.

The possibility of this condition being responsible for a maternal obstetric palsy should be considered before the defect is assumed to have resulted from a lumbosacral plexus injury occasioned by the foetal head or forceps.

*G. de M. Rudolf*

## NEUROMUSCULAR DISEASES

1513. **The Effect of Changes in Serum Potassium upon Myotonia**
P. LEYBURN and J. N. WALTON. *Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Neurosurg. Psychiat.]* **23**, 119–126, May [received July], 1960. 1 fig., 14 refs.

It has previously been reported that myotonia is lessened by administration of an ion-exchange resin, which lowers the serum potassium level. The authors, working at the Royal Victoria Infirmary, Newcastle upon Tyne, have tried this treatment in 7 patients, 5 of whom had dystrophia myotonica and 2 myotonia congenita. The resin was sodium polystyrene sulphonate and the treatment was continued for 15 to 24 days. In 3 cases

the authors observed no consistent fall in the serum potassium level and no improvement in the myotonia. In the remaining 4 patients there was progressive reduction in the serum potassium level and objective testing showed a slight reduction of myotonia in 3 and more marked improvement in one. None of the patients, however, noticed any subjective improvement. The authors conclude that ion-exchange resins of this type are of no practical value in the treatment of myotonia.

*J. W. Aldren Turner*

1514. **The Electromyogram from Ocular Muscles in Myasthenia Gravis**

M. L. Sears, F. B. Walsh, and R. D. Teasdall. *A.M.A. Archives of Ophthalmology* [*A.M.A. Arch. Ophthal.*] **63**, 791–798, May, 1960. 4 figs., 22 refs.

The authors of this paper from the Johns Hopkins University School of Medicine and Hospital, Baltimore, describe an electromyographic study of the action potentials from involved ocular muscles in patients with myasthenia gravis. None of the 7 patients examined had symptoms suggestive of thyrotoxicosis and 3 were euthyroid. In all the patients there was a progressive decline in amplitude and frequency of the discharge on sustained contraction of the horizontal rectus oculi muscles. These changes preceded any visible evidence of fatigue when horizontal gaze was maintained. An interval of rest in the primary gaze position, even for a few seconds, was sufficient to restore the discharge pattern to the pre-fatigue level. A similar restoration occurred following intravenous injection of edrophonium chloride (" tensilon "). In 5 patients the electromyogram suggested that some irreversible changes had already taken place in the extra-ocular muscles.

*D. P. Greaves*

## DISSEMINATED SCLEROSIS

1515. **Studies on Intermediate Carbohydrate Metabolism in Multiple Sclerosis**

B. McArdle, I. C. K. Mackenzie, and G. R. Webster. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **23**, 127–132, May [received July], 1960. 12 refs.

It has been suggested that in disseminated sclerosis there is a defect in the Krebs cycle. The authors of this paper from Guy's Hospital Medical School, London, set out to investigate this hypothesis, employing specific methods for estimating the blood levels of α-ketoacids and pyruvate following the ingestion of glucose in 41 patients suffering from disseminated sclerosis. The existence of an abnormality of pyruvate metabolism in some cases of the disease was established. This was expressed as an increase in pyruvate tolerance, a raised blood level of α-ketoglutarate following the ingestion of glucose, or a lowered blood citrate level. There was little indication that these abnormalities were in any way related to the state of progression of the disease; they tended rather to be associated with the severity of spasticity or with malnutrition. In some cases malnutrition was a consequence of the severe trigeminal neuralgia which is occasionally a complication of disseminated sclerosis.

The authors conclude that these metabolic disturbances are probably not causally related to the neurological disease.

*J. B. Cavanagh*

1516. **Field Investigations into the Spread of Disseminated Sclerosis in Spessart and the Neighbouring District.** (Felduntersuchungen über die Verbreitung der Multiplen Sklerose im Spessart und dem benachbarten Siedlungsraum)

H. Bammer. *Münchener medizinische Wochenschrift* [*Münch. med. Wschr.*] **102**, 1115–1119, May 27, 1960. 15 refs.

The author describes from the University of Würzburg a field study of the incidence of disseminated (multiple) sclerosis (D.S.) in the rural district of Spessart, this being chosen since the intensive study of a small district allows all relevant factors in the environment and heredity to be fully assessed in investigating the aetiology of such a disease as D.S. All patients reporting with symptoms of the disorder since 1937 were included in the study and reassessed to establish a firm diagnosis.

At the beginning of 1958 there were 94 cases per 100,000 population. From the point of view of social welfare it can be assumed that there is one case of D.S. per 1,000 inhabitants; this figure is compared with those of previous studies. Morbidity was calculated as the number of new cases per annum per 100,000 population, a mean of 5 cases per 100,000 being established for the years between 1937 and 1958. Study of the relation between incidence and size of the community showed that a relatively higher proportion of cases occurred in small villages; the highest incidence was found among agricultural and forestry workers, who showed a rate of 13 per 10,000 as compared with the over-all rate of 6 per 10,000. The degree of purity or contamination of drinking water did not affect the incidence, but the poor or non-existent sewage system common in all country districts had a definite relationship, which is not yet understood, to morbidity of D.S. The influence of close spatial or personal contact between patients before illness was next investigated and found to be relevant, and several examples are quoted [but the statistical significance of this finding is not mentioned]. The incidence of D.S. among blood relatives of patients was found to be no higher than the incidence among relatives by marriage. A special study in a small highly inbred community showed that the incidence of D.S. was no higher than elsewhere. In the author's view these last two findings throw doubt on the notion that genetic factors are concerned in the aetiology of the disease. Further the author was able to show that patients with D.S. were living nearer each other at the time the disease appeared than they were at birth.

It is concluded that this study emphasizes the role of exogenous factors as opposed to that of genetic factors in the pathogenesis of disseminated sclerosis, and also that exposure to environmental factors best explains group diseases.

*M. R. Medhurst*

# Psychiatry

1517. **Recognition of Emotional Disturbance and the Prevention of Suicide**
A. CAPSTICK. *British Medical Journal* [*Brit. med. J.*] **1**, 1179–1182, April 16, 1960. 13 refs.

The author has examined the coroner's records in 881 cases of suicide (589 males and 292 females) investigated during the period 1951–5, with a view to discovering signs recognizable as danger signals calling for medical help which might prove of value in considering methods of prevention. He found that 78·2% of these subjects had been under a doctor's care in the months preceding the suicide, the symptoms complained of being those associated with emotional illness, such as headache and depression. The records also showed that 92 had recently been in a mental hospital; the most dangerous time for suicide was immediately after discharge from hospital. Many were depressed just before the final act. Other groups were the emotionally unstable, those worried by domestic difficulties, and some who had been involved in quarrels just before death. On the other hand 306 had seemed normal, and even showed improvement from a pre-existing depression, before committing suicide. The author considers that the intention to commit suicide was present in these cases, even though they seemed outwardly calm, rather than that they acted on sudden impulse. "Suicide notes" were left by 136 persons, more often by the younger suicides. Of these about half gave inability to tolerate a painful situation as the reason for the act, while physical illness was mentioned by the older people, but business and financial difficulties rarely (9 cases). While 79 notes gave an explanation of what the writer wanted to escape from, only 30 indicated where they believed they were going. The author does not consider that a belief in an afterlife is a powerful determinant in suicide. In 16 instances the suicide note was wounding or malicious.

The author concludes that psychiatric treatment cannot prevent all suicides, but that many of these persons might have been helped if it had been given in time. There is a special need for vigilance immediately after discharge from hospital, and suicide threats should receive more attention than they generally do at present.

*Gavin Thurston*

1518. **Psychology and Psychopathology of Patients after Extirpation of the Larynx.** (Psychologie und Psychopathologie Kehlkopfexstirpierter)
H.-J. HAASE. *Fortschritte der Neurologie, Psychiatrie und ihrer Grenzgebiete* [*Fortschr. Neurol. Psychiat.*] **28**, 253–272, May, 1960. 15 refs.

The author reports from the Medical Academy, Düsseldorf, the results of the psychological examination of 40 male patients who had undergone extirpation of the larynx for carcinoma and who were examined 6 months or more after the operation; their ages ranged from 40 to 80 years. The commonest mental change, which was observed in over half the patients, was an increased irritability, due in most cases to the restriction of the cathartic function of speech. In 17 patients other changes were found; thus half of them displayed signs of self-depreciation, these taking the forms of feelings of inferiority, suspiciousness, touchiness, inhibitions, and jealousy; the reasons for the feelings of self-depreciation varied from case to case, and in some of these patients self-respect was regained after learning pharyngeal speech. The other half of this group of patients suffered from depressive moods; here again the content of the mood changes were conditioned by the pre-morbid personality and life history. In 2 patients pre-morbid antisocial trends became accentuated, but in 7 others the personality change was in the opposite direction and they became more relaxed. Of these last, 3 continued in their previous occupations, 3 could not do so, and the other was an old age pensioner. All these 7 patients had been syntonic, restrained people all their lives and possessed the high regard of their families.

The investigation showed that in the interplay between environmental and constitutional factors it was the latter which, on the whole, asserted themselves.

*J. Hoenig*

1519. **Falling Asleep Open-eyed during Intense Rhythmic Stimulation**
I. OSWALD. *British Medical Journal* [*Brit. med. J.*] **1**, 1450–1455, May 14, 1960. 9 figs., 17 refs.

Writing from the University of Edinburgh, the author describes experiments carried out at the Institute of Experimental Psychology, Oxford, which followed Sargant's interpretation of Pavlov's theory of internal inhibition—defined by him as the inhibition "evoked in the cerebral cortex by any sensory stimulus to which from the point of view of the dog's general economy or well-being, it was better that the dog should not respond". Pavlov identified internal inhibition with sleep. Among the causes of internal inhibition are "transmarginal" stimuli and excessively intense repeated stimuli. Sargant has interpreted the collapse and trance states occurring in human subjects after great excitement as manifestations of "transmarginal inhibition", which he regards as a protective mechanism.

In the present experiments performed on 4 male healthy volunteers with a normal electroencephalogram (EEG) the subjects' eyes were fixed open and the EEG and electrocardiogram (ECG) recorded by means of stick-on electrodes on the scalp and arms. In the first experiment (3 subjects) loud rhythmic ("blues") music was played, and synchronously with the rhythm of the music the subjects (1) received electric shocks to the left lateral popliteal nerve sufficient to cause sharp eversion of the foot, or (2) were brightly illuminated by four 60-watt electric light bulbs 2 feet (60 cm.) above the open eyes.

Despite this the alpha rhythm appeared in the EEG of all 3 subjects after 5 to 10 minutes and subsequently slowed and disappeared; the flat EEG tracing typical of light sleep was present after 8 to 12 minutes and persisted for 15 to 30 minutes. In all 3 also the pupil contracted and all were aware of having been " asleep ". In the second experiment (2 subjects) the same loud music was again played and the same synchronous visual stimulation (but not the electric shocks) given; in this test the subjects were asked to bang both arms actively up and down from the elbow and to tap both feet in time to the music and the flashing lights. In both subjects the alpha rhythm began to appear after approximately 7 minutes. One subject stopped moving temporarily after 10 minutes, and during the next 15 minutes stopped all active movement on 65 occasions, the EEG at these times being characteristic of light sleep lasting for periods of 3 to 20 seconds. The second subject had a similar episode after 15 minutes and 52 further episodes over the next 25 minutes. Neither subject was aware that he had stopped moving more than once or twice.

It is concluded that the quality of thinking and attention can be reduced to a level similar to that in the sleeping state by intense monotonous stimulation with the eyes fixed open, possibly because of habituation of the reticular activating system. It is suggested that this physiological response could prove dangerous for drivers of cars and lorries and people working with machinery and that mental efficiency may be very much lowered among people working in monotonous noisy conditions.

*Christopher Wardle*

1520. **Relation of Rorschach Factors and Plasma Hydrocortisone Level in Hypnotically Induced Anxiety**
E. E. LEVITT and H. PERSKY. *Psychosomatic Medicine* [*Psychosom. Med.*] **22**. 218–223, May–June, 1960. 11 refs.

At the Institute of Psychiatric Research, Indiana University Medical Center, Indianapolis, the authors have investigated the relationship between plasma hydrocortisone (P.H.C.) level and a group of indices derived from the Rorschach test in patients during a hypnotically induced state of anxiety. A previous investigation (Persky *et al.*, *Arch. Neurol. Psychiat.*, 1958, **79**, 434) had shown that hypnosis constituted a reliable means of producing a " pure " anxiety state and that raised P.H.C. levels were correlated with such anxiety. The method involved the hypnotic induction of anxiety in 12 normal subjects (6 male, 6 female), in each case the " anxiety phase " being preceded by a " non-anxiety phase " under hypnosis. Amnesia for each phase was separately induced. A Rorschach test was administered and a blood sample taken during each phase and also at the end of the total procedure, the P.H.C. level being estimated by the method of Nelson and Samuels.

A significant positive or negative correlation was established between an increase in P.H.C. level and 3 out of 26 factors in the Rorschach test, pure C (colour) being positively correlated with such increase while P (popular response) and F+% (percentage of good form response) were negatively correlated with a rise in P.H.C. level. Another 5 Rorschach indices which are generally recognized to be correlated with neurotic anxiety were not found to be significantly associated with changes in P.H.C. levels. The findings in respect of pure C, P, and F+% reflect a more shattering type of anxiety which the authors consider to be pre-psychotic in nature. It is concluded that pre-psychotic rather than neurotic grades of anxiety are associated with changes in the plasma level of hydrocortisone. *A. Balfour Sclare*

1521. **The " Brain Fag " Syndrome in Nigerian Students**
R. PRINCE. *Journal of Mental Science* [*J. ment. Sci.*] **106**, 559–570, April [received June], 1960. 7 refs.

It would appear that a high proportion of patients seen in psychiatric clinics in Nigeria are students and teachers, and the author suggests that this proportion is higher for Nigeria than for Western countries, although no figures are available. He describes a distinct syndrome which, he states, is very common among Nigerian " brain-workers ", and makes some general observations on the basis of 10 cases investigated.

The " brain fag " syndrome, as here described, is characterized by complaints of difficulty in concentration and of impairment of grasp, subjective loss of memory, and various somatic symptoms mainly of pain or paraesthesiae in the head and neck, and visual disturbances. The syndrome is commonly observed in adult unmarried Nigerian males between the ages of 15 and 30, who are students or teachers or clerks undertaking postgraduate studies. Insomnia, anorexia, and depression are apparently exceptional in the series. The symptoms usually developed during periods of intensive study; in some cases they were of short duration, in others they persisted. [Unfortunately the author describes no more than 4 case histories, and these only in outline.]

Discussing some possible aetiological factors the author states that genetic differences, intelligence, parental literacy, and study habits do not appear to be directly related to the occurrence of the syndrome, and proposes an explanation in psychodynamic terms—a reaction of the Nigerian personality to European learning techniques.

*R. H. Cawley*

1522. **Critical Ages for Maternal Bereavement in Psychoneuroses**
H. BARRY JR. and E. LINDEMANN. *Psychosomatic Medicine* [*Psychosom. Med.*] **22**, 166–181, May–June, 1960. 4 figs., 20 refs.

At the Department of Neurology and Psychiatry, Harvard Medical School, and Massachusetts General Hospital, Boston, an investigation was undertaken with the aim of discovering whether loss of the mother during early life was significantly correlated with the subsequent development of psychoneurosis. Previous literature indicates such an association in regard to psychosis, but the results of studies of this association in psychoneurosis have been controversial. The subjects were 937 patients (395 male and 552 female) seen between 1944 and 1953 because of psychoneuroses or psychosomatic disorders and their records were reviewed with special reference to the occurrence of parental death, separation, or divorce.

If the mother or father had died or gone away the age of the patient at the time of such loss was noted. The death rates for mothers and for fathers were calculated separately for male and female patients. Although there was no matched control group control, figures were obtained from published data for the general population.

It was found that the maternal death rate among the psychoneurotic subjects was significantly higher than in the general population. This was especially true of the female patients, of whom 12% had lost their mothers during childhood (compared with 7% of males). The critical age period for the impact of such bereavement in girls appeared to be during the first 3 years of life. The death rate for fathers followed a pattern similar to that in the general population. Where the deprivation took the form of separation or divorce of the parents, the results were similar to those arising from death of the mother. It is suggested that the term " broken home " should be dropped and that it should be replaced by more specific categories such as maternal bereavement or parental divorce.

[The sample studied contained an unspecified number of " psychosomatic disorders ". The latter are generally considered to be nosologically different from the psychoneuroses.] *A. Balfour Sclare*

## SCHIZOPHRENIA

1523. **Phenothiazine Derivatives in the Treatment of Schizophrenia.** [Review Article]
L. HURST. *Journal of Mental Science* [*J. ment. Sci.*] **106**, 755–770, April [received June], 1960. Bibliography.

1524. **Chlorpromazine and Pecazine in Chronic Schizophrenia**
L. HURST. *Journal of Mental Science* [*J. ment. Sci.*] **106**, 726–731, April [received June], 1960. 13 refs.

In this double-blind controlled trial carried out at Shenley Hospital, Hertfordshire, on 92 female chronic schizophrenic in-patients to compare the effects of chlorpromazine, pecazine, and a placebo, the patients were divided into three groups, one receiving the placebo throughout, and the other two, after a preliminary period of placebo treatment, having 8-weekly periods of the two drugs alternately. Assessment was carried out every 4 weeks using the modified Albany Behavioural Rating Scale.

At the end of 8 weeks patients in both groups receiving the drugs were somewhat better than patients in the control group, those receiving chlorpromazine significantly so. Using each patient as her own control, only slight improvement was shown throughout the period by those starting the trial on pecazine, whereas those starting with chlorpromazine showed improvement approaching significant level at the end of the 8th week, and this improvement continued into the first 4 weeks of treatment with pecazine, but thereafter deteriorated. There was no significant change in the scores for mental tension or thought disorder during the tests. In the over-all result only 7 out of 61 patients showed an improvement of more than 3 points out of a possible 18 while receiving chlorpromazine. It is suggested that phenothiazine derivatives are used too frequently in the treatment of chronic schizophrenic in-patients. One patient developed agranulocytosis while taking pecazine.

*E. H. Johnson*

1525. **Predicting the Outcome of a Schizophrenic Episode**
R. G. WALKER and F. E. KELLEY. *A.M.A. Archives of General Psychiatry* [*A.M.A. Arch. gen. Psychiat.*] **2**, 492–503, May, 1960. 16 refs.

The study here reported from the Veterans Hospital, Brockton, Massachusetts, is part of a large country-wide project now being carried out at mental hospitals within the U.S. Veterans Administration. In 225 male schizophrenic patients aged 20 to 59 years a number of demographic variables and symptoms present on admission were compared with the outcome of the disorder. The initial diagnosis was determined by the level of thought disorder, withdrawal, suspicion and the presence of auditory hallucinations or delusions; 107 cases were classified as acute and 118 as chronic schizophrenia. The demographic factors considered were age, educational level, marital status, sub-diagnosis, severity of illness, record of previous psychiatric hospital admissions, and employment history. Outcome was assessed in the acute patients, both by whether or not the patient was discharged from hospital within 6 months, and by his recovery from certain rateable schizophrenic symptoms, such as withdrawal, disorientation, thought disorder, auditory hallucinations, delusions, depression, anxiety, hostility, and lack of goals. In the chronic group of patients, where symptom rating was not possible, outcome was assessed by length of hospital stay (more or less than 6½ years) and whether or not the patient had been re-admitted within a year of discharge.

In the acute group 2 of the demographic variables appeared to be significantly related to outcome. Thus a higher educational level and greater time spent previously in hospital were both favourable factors and were associated with a shorter subsequent stay in hospital. Among symptoms, disorientation alone was significantly related to outcome and was associated with a longer stay in hospital. None of either group of variables was related to " symptom recovery ". Two aspects of treatment were investigated as possible influences upon outcome: (1) patients given short-term psychotherapy stayed longer in hospital than a group of controls not so treated, but did appear to differ in rate of recovery; (2) treatment with chlorpromazine, whether in a dosage of more or less than 400 mg. per day, made no difference to the outcome. In the chronic group, apart from age, which was negatively related to length of stay, the results paralleled the findings in the acute group. Certain background variables were related to time spent in hospital, but not to recovery as measured by re-admission (or not) within a year of discharge. When the latter criteria of recovery were applied, that is, period of stay in hospital and re-admission within a year, the findings in a small group of 27 more recently admitted patients with acute schizophrenia were similar to those in the large group. *J. S. Bearcroft*

1526. **Studies of Thought Disorder in Schizophrenia. I. Chapman's Tests of Distractibility and Associative Intrusion in Schizophrenia and Organic Brain Disease**
I. FEINBERG and M. MERCER. *A.M.A. Archives of General Psychiatry* [*A.M.A. Arch. gen. Psychiat.*] **2**, 504–511, May, 1960. 1 fig., 5 refs.

The results of tests of cognitive function in schizophrenic patients mostly fall intermediately between those of normal subjects and those of patients with organic brain disease, but there is always a considerable overlap. The authors, working at the U.S. National Institute of Mental Health, Bethesda, Maryland, were concerned to find a test of cognitive function which would qualitatively differentiate schizophrenia and organic illness, and in this paper they report the results obtained with the tests of distractability and associative intrusion devised by Chapman (*J. abnorm. soc. Psychol.*, 1958, **56**, 374). The 16 patients with organic disease were mostly elderly (mean age 69·6 years) and suffering from vascular insufficiency and loss of memory for recent events, with usually also other features such as defects in orientation, comprehension, and judgement. The 42 schizophrenic patients, who were younger (mean age 29·5 years), were divisible into chronic and relatively acute groups, determined by whether they had been in-patients for more or less than 3 years. The distractability test consisted of matching picture cards (illustrated) on the grounds of specific features while ignoring certain other likenesses depicted on the cards. The associative intrusion test was similarly designed, but consisted of matching words, the subject being asked to associate specific concepts and reject other similarities. It was possible to compare these two groups of patients, not only in terms of overall accuracy, but also in respect of the nature of the errors.

In the distractability test the performance of the organic group of patients was consistently worse than the schizophrenic group in that they made more distraction errors or wrong associations; the results were similar in the association intrusion test. When a correction was made for differences in I.Q. levels the disparity, though less marked, was still evident. Duration of the schizophrenia had no effect upon results. On the other hand the pattern of error scoring was similar in the two groups and it was apparent that difficulty in recall played a part in the poor performance of some of the patients with organic disease, although severe memory loss had been a disqualifying factor in a pre-test.

The authors conclude that these two tests do not measure a disturbance of thought which is specific to schizophrenia. *J. S. Bearcroft*

1527. **Perception of Hidden Pictures by Schizophrenic Patients**
T. E. WECKOWICZ. *A.M.A. Archives of General Psychiatry* [*A.M.A. Arch. gen. Psychiat.*] **2**, 521–527, May, 1960. 25 refs.

The ability to select relevant and disregard irrelevant information is discussed in terms of Gestalt psychology. It is possible to test this function by means of drawn figures hidden in a background of other irrelevant figures; the figures may be embedded in or overlapped by the surrounding material. This function has often been found to be impaired in patients with an organic brain lesion and particularly in those patients who are also suffering from aphasia. This suggests that the disability is one affecting the symbolic processes underlying speech and thinking. It is postulated that these same processes of concept formation are also affected in schizophrenia and that therefore in performing a Figure-Ground Confusion test schizophrenic patients would encounter difficulty.

Two sets of pictures were shown to 176 subjects, including groups of acute and chronic schizophrenic patients, patients with organic brain disease, patients with functional psychiatric illness other than schizophrenia, and finally a group of normal subjects. The first set of pictures depicted common objects, such as a knife and fork overlapped or hidden by jumbled lines producing figure-ground confusion. The second set depicted the same objects without the superimposed lines and was intended to exclude patients failing to co-operate or unable to identify the objects. The patients were also subjected to a general intelligence test.

No difference was found between the performances of the normal controls and the "functional" group. Schizophrenic patients gave a poorer performance than either the normal or functional groups, but a better performance than patients with organic brain lesions. Though there was a positive correlation between performance and intelligence in the schizophrenic patients and though intelligence was inferior in the schizophrenic patients compared with the functional group, when these two groups were matched for intelligence, sex, age, and length of stay in hospital, the schizophrenic patients' performance was still significantly inferior to that of the "functional" group. It is suggested that this ability to select and disregard according to certain criteria is part of cognitive function and that it is affected in patients suffering from schizophrenia (less in the acute schizophrenic than in the chronic), though less markedly affected than in patients with organic brain lesions.
*J. S. Bearcroft*

1528. **Effects of Triiodothyronine in Schizophrenic Patients: Correlations of Changes in Basal Metabolism with Urinary Creatine and Cholesterol and Tocopherol Levels in the Blood**
B. J. MEYER, B. CENTURY, A. C. MEYER, and M. K. HORWITT. *A.M.A. Archives of General Psychiatry* [*A.M.A. Arch. gen. Psychiat.*] **2**, 528–533, May, 1960. 5 figs., 18 refs.

Pursuing their previous work at the Elgin State Hospital, Elgin, Illinois (*A.M.A. Arch. gen. Psychiat.*, 1959, **1**, 372) on the effects of triiodothyronine on the psychiatric and biochemical status of schizophrenic patients, the authors now present a study of the changes in the serum cholesterol and plasma tocopherol levels and urinary creatine excretion in relation to the basal metabolic rate (B.M.R.). They point out that there is no evidence giving reason to suppose that such findings would differ from those observed in non-schizophrenic subjects.

Observations were made on 11 experimental and 6 control subjects, all euthyroid male chronic schizophrenics who had been receiving a controlled diet for more than 4 years and for whom monthly biochemical base-line values were available. Approximately half the members of each group had been kept on a low-tocopherol diet during this period. The experimental group received 100 μg. of triiodothyronine daily for 18 days, no drug for the next 24 days, and then 200 μg. daily for a further 30 days.

Since the results did not seem to be affected by the plasma level of tocopherol, all other data from the two dietary groups were pooled. Slight to moderate weight loss was seen by the end of the first week of each treatment, but this was mostly regained within 16 weeks of the end of treatment. The B.M.R. rose by an average of 14·5 units with a daily dose of 100 μg. of triiodothyronine and by a mean of 23 units with 200 μg. daily, but there were considerable individual differences. The over-all increase in the B.M.R. was always paralleled by a fall in the serum cholesterol and plasma tocopherol levels, suggesting that such changes were non-specific and secondary to the general decrease in the plasma lipid level. The average daily excretion of creatine (0·09 g.) rose to a significant extent in only 4 patients treated with 100 μg. of triiodothyronine daily, but with a dose of 200 μg. a day 8 of the 11 patients excreted up to 0·35 g. daily. These increases were temporary and returned to near normal values during the course of each treatment. No reciprocal decrease in urinary creatinine excretion was apparent.

[The relation of these findings to those in non-schizophrenics is not made explicit.] *Alan A. Black*

1529. **Experimental Sleep Deprivation in Schizophrenic Patients**

E. K. Koranyi and H. E. Lehmann. *A.M.A. Archives of General Psychiatry* [*A.M.A. Arch. gen. Psychiat.*] **2**, 534–544, May, 1960. 5 figs., 22 refs.

Previous workers have described the effects of sleep deprivation on animals and normal human subjects. The present paper, from the Verdun Protestant Hospital and McGill University, Montreal, reports the effects of 100 consecutive hours of wakefulness on 6 male chronic schizophrenics, of whom 2 were paranoid, 2 catatonic, and 2 hebephrenic. These volunteer patients had a good relationship with the staff, some members of which were continuously with the patients observing, testing, and engaging them in social and physical activities during the study.

Over the first 3 days group cheerfulness and solidarity were predominant, though interspersed with periods of irritability, somnolence, and withdrawal. During the 4th day there were signs of increased psychological and physiological impairment and loss of group cohesion. Each individual's psychopathology became more pronounced and 5 of the 6 patients showed behaviour closely resembling that of the acute psychotic phase present at their first admission. By the morning of the 5th day patients were unable to sustain the effort to perform the simplest task and when eventually allowed to sleep did so for 10 to 12 hours. Most of the results of the experiment were in the expected direction, for example, an initial fall followed by a rise in the eosinophil count, a decrease in pulse pressure and systolic blood pressure, increase in weight, decrease in tapping speed, and increased reaction time. Unexpectedly, the pulse rate and temperature rose and the appearance of delta waves in the electroencephalogram, reported by other workers, was not seen.

At the end of the experiment the patients were divided into 2 groups, each containing one paranoid, one catatonic, and one hebephrenic patient. One group of 3 was returned to the habitual hospital environment after waking, whereas the other 3 patients were kept somnolent with chlorpromazine for the next 4 days, after which 2 of them improved and received further intensive treatment. Six years later all the patients are still in hospital. However, those who received chlorpromazine experimentally have improved remarkably and are ready for discharge, while the other 3 are essentially unchanged. The authors discuss the possibility of determining the "remission potential" of chronic schizophrenic patients from observation of their biological response to stress, but acknowledge that no valid conclusion can be drawn from such a small sample. *Alan A. Black*

## TREATMENT

1530. **Five-Year Follow-up of Results of Reserpine Therapy in Mental Hospital Practice**

R. Maggs and R. M. Ellison. *Journal of Mental Science* [*J. ment. Sci.*] **106**, 590–598, April [received June], 1960. 23 refs.

Reserpine was tried in the treatment of 180 patients (74 male and 106 female) at Hellingly Hospital, Hailsham, Sussex. The diagnoses were schizophrenia in 111, manic-depressive psychosis in 31, neurosis in 18, and other conditions in 20. The authors did not use a blind technique for elimination of selective bias and there were no controls. The patients were given what was considered to be an adequate course of treatment, and those who responded significantly were kept on a maintenance dosage and followed up for periods of 3 to 5 years. The patients were assessed as much improved, improved, or not improved at the end of the course of treatment lasting 6 to 8 weeks. In the first 40 patients who received reserpine in a daily dosage of 1·5 mg. there was no significant improvement. When a higher dosage of 12 to 15 mg. daily was given to 162 patients a number of remissions occurred.

[The results are difficult to evaluate because of the lack of controls.] The authors describe 2 striking cases (both in females) of catatonic schizophrenic illnesses of 7 and 15 years' duration respectively, characterized by homicidal impulses, aggressiveness necessitating frequent seclusion, and gross thought disorder. On reserpine therapy both patients improved sufficiently to be discharged from hospital and to support themselves in the community. The improvement was sustained in each case. Of the 111 schizophrenics receiving high

doses of reserpine 17 were described as much improved and 40 as improved. Of the remaining 51 patients, none was much improved and 14 were improved. Side-effects of the drug, which occurred in over 50% of the patients, appeared to be reversible and were not related to the dosage. One patient committed suicide during treatment and in one, who died, acute yellow atrophy developed.

The authors conclude that reserpine is of value in mental hospital practice in cases of schizophrenia in which there is florid psychotic behaviour. They state that an adequate dosage is 8 to 15 mg. daily for 6 to 8 weeks, followed by a maintenance dosage of 1 mg. three times a day. *R. H. Cawley*

1531. **Phenelzine (" Nardil ") in the Treatment of Endogenous Depression**
J. T. HUTCHINSON and D. SMEDBERG. *Journal of Mental Science* [*J. ment. Sci.*] **106**, 704–710, April [received June], 1960. 3 figs., 9 refs.

In a double-blind, cross-over trial carried out in 2-weekly stages at Cane Hill Hospital, Coulsdon, Surrey, phenelzine ($\beta$-phenyl ethyl hydrazine; "nardil") was given to 34 female in-patients aged 26 to 77 suffering from depression. All the patients had previously had electric convulsion therapy for recurrent attacks of depression, which had been present for an average period of 8 years.

Assessment of the results in respect of 14 items on a 4-point scale showed that there was marked improvement in 13 patients (of whom 9 could be discharged from hospital), moderate or slight improvement in 14, little change in 2, while 5 patients were worse. Early waking in the morning and inability to sleep, which were constant symptoms in the series, gave a valid response to the drug as compared with the placebo. It was noted that constipation and loss of appetite responded remarkably to the placebo. From the facts that there were no side-effects during the 4 weeks of the trial and that the drug exerted an obvious positive effect on some of the physiological aspects of depression it is concluded that phenelzine has a place in the treatment of depression.
*E. H. Johnson*

1532. **A Long-term Investigation of Chlorpromazine**
N. W. WINKELMAN JR. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **116**, 865–869, April, 1960. 4 refs.

From the University of Pennsylvania School of Medicine, Philadelphia, the author presents the results of his 6-years' experience in the treatment with chlorpromazine of 75 psychiatric patients, and discusses methods and theories of treatment. He believes that it is necessary to understand the patient's conflicts and personality structure to ensure satisfactory use of the drug. The effect of chlorpromazine is either to suppress painful conflicts and instinctive drives or else to help him to accept them by reliving memories of the conflict. When suppression is indicated the dose will depend upon the strength of the instinctive drive, while when acceptance is desired the therapeutic relationship is of prime importance and the role of the drug is to help to bring unconscious material to consciousness. Chlorpromazine tends to diminish the influence of both primary drives and the super-ego. A relative increase of ego strength and its defences ensue, with improved reality testing. The dosage required will be high where it is hoped to suppress drives, but a knowledge of underlying dynamics is essential. The dose must be raised when there is increased stress from either internal conflicts or from environment. The intention in both neurotics and psychotics should be strengthening of the ego.

The results in the 75 patients were excellent, nearly all remaining symptom-free throughout the 6 years. When the drug was discontinued in a number of cases a partial return of symptoms was noted within 5 to 12 days. Complications included 7 cases of liver damage, which occurred early in the course, and mild weight gain. For more permanent relief of symptoms psychotherapy was a necessary adjunct. *J. S. Bearcroft*

1533. **Imipramine (Tofranil) in Mental Health Clinic and Private Practice**
B. V. EARLE and A. M. EARLE. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **83**, 804–806, Oct. 8, 1960. 15 refs.

1534. **The Treatment of Psychopaths**
P. D. SCOTT. *British Medical Journal* [*Brit. med. J.*] **1**, 1641–1646, May 28, 1960. 36 refs.

The author of this paper from the Maudsley Hospital, London, points out that nothing is gained by attempting to distinguish chronic offenders and psychopaths. In clinical practice, psychopathic traits are often seen to coexist with guilt feelings and neurotic symptoms. Some such traits occur in a wide range of individuals who are not psychopathic, and many individuals whose behaviour is persistently antisocial show few of the psychopathic personality traits.

Excluding the psychotic and the organically ill, chronic offenders may be classified into 4 somewhat over-lapping groups. (1) Those trained to antisocial standards; they have normal personalities and are adequately adjusted but to a delinquent subculture. (2) Those whose behaviour is reparative, compensating for personal difficulties or handicaps; arrogantly antisocial conduct as a consequence of inferiority feelings or homosexual conduct as a result of unconscious fear of women is seen in this type. (3) The untrained, whose upbringing has been so disorganized or inconsistent that they have never acquired a coherent pattern of conduct; they are diffusely impulsive and irresponsible from an early age. (4) Those with rigid fixations whose learning pattern has broken down as a result of extreme stress in early life; their behaviour resembles the inappropriate, stereotyped reactions of experimental animals confronted with insoluble problems; they persist in the same irrational offences despite severe punishment and are bewildered by their own behaviour, which seems aimless and fails to arouse sympathy.

These subdivisions are important because they correspond to radically different treatment requirements.
*D. J. West*

# Dermatology

1535. **Tinea Capitis Treated with Griseofulvin**
R. H. MEARA. *British Journal of Dermatology* [*Brit. J. Derm.*] **72**, 169–172, May, 1960. 1 fig., 1 ref.

The successful results obtained with griseofulvin by mouth in the treatment of tinea capitis (Williams *et al.*, *Lancet*, 1958, **2**, 1212) led the author to give this antibiotic to all children admitted to the ringworm unit of the Goldie Leigh Hospital, London. A total of 31 children were treated, the infecting organisms being *Microsporum audouini* in 24, *M. canis* in 4, and *Trichophyton rubrum*, *T. discoides*, and *T. violaceum* in one each. The antibiotic was given in a dosage ranging from 0·125 g. twice daily in younger children to 0·25 g. 3 times daily in older children. Administration was continued until most of the infected hairs showed a normal zone proximal to the infected part when the hair was clipped off close to the scalp. The duration of treatment varied from 7 days (one case) to 5 weeks. No local treatment was given. All the children were followed up for not less than 2 months after they were considered free from infection. Cure was obtained in all cases, although in 3 a relapse occurred 3 to 4 weeks after treatment ceased. A second course of griseofulvin resulted in cure in these 3 cases and in 2 others in which infected stumps persisted throughout the first course. Treatment was well tolerated. There were no side-effects apart from an absolute depression of the polymorphonuclear leucocyte count in 2 patients receiving relatively large doses for their age; the counts rose to normal a few days after withdrawal of the drug. No blood changes were observed when the daily dose of griseofulvin was subsequently reduced to 0·25 g. in a young child and 0·375 g. in older children. *Benjamin Schwartz*

1536. **The Treatment of Favus with Griseofulvin**
H. KOPP, S. A. KVORNING, and P. V. MARCUSSEN. *British Journal of Dermatology* [*Brit. J. Derm.*] **72**, 173–178, May, 1960. 12 refs.

Favus is endemic in the Arctic regions of Greenland and because of unfavourable environmental conditions it has been difficult to eradicate the infection. The possibility of treating the condition by oral administration of griseofulvin was therefore explored, and in an initial trial 8 patients (2 children and 6 adults) from Northern Greenland were treated at the Finsen Institute, Copenhagen. The antibiotic was given in a daily dosage of 1 g. in adults and 0·5 g. in children for periods ranging between 70 and 78 days. In all cases the hair was closely cropped each week and in 4 cases x-ray epilation was carried out in addition. No local treatment of any kind was given.

The scutula had disappeared after the 40th day and there was no suspicious scaling after the 54th day. Cultures were negative by the 33rd day and potash preparations negative after the 48th day. Cure was obtained in all the cases, there being no significant difference in this respect between the epilated and non-epilated cases. Initially *Penicillinum brevicaule* was isolated from two nails, but this was not demonstrable after 12 days' treatment. *Trichophyton schoenleini* was found in one nail when it was removed after clinical and cultural cure following 57 days' treatment. There were no toxic side-effects or pathological changes in the fundus oculi or blood picture, but in 3 patients trichophytide eruptions developed after 12 to 28 days; these eruptions subsided quickly in spite of continued treatment.

*Benjamin Schwartz*

1537. **Griseofulvin and Favus: a Report on Work in Progress**
J. H. S. PETTIT. *British Journal of Dermatology* [*Brit. J. Derm.*] **72**, 179–184, May, 1960. 11 refs.

The author of this paper from the University of Shiraz, Iran, describes the results obtained with griseofulvin in the first 50 cases (out of a much larger number) of favus infection. The average dosage was 1 g. daily for all patients over the age of 12 years, 750 mg. for those aged 7 to 12, and 500 mg. for those under 7 years.

In general treatment was continued for 4 weeks, although in some cases one to 3 weeks were enough. No dramatic change was observed during the first week of treatment but some improvement was noted by the end of the second, and non-fluorescent roots of contaminated hairs could be seen during the third week, after which the hair was shaved. Of 38 patients followed-up for more than 3 months all except 5 were cured; from the case histories of these 5 it appeared that in 4 there had been reinfection. The remaining 12 patients were clinically cured 2 to 8 weeks after cessation of treatment, but these cases were followed-up for under 3 months.

No adverse side-effects were encountered, although papular urticaria developed in one child and meningococcal meningitis in another, neither of these two conditions being considered to be aetiologically related to administration of griseofulvin. *Benjamin Schwartz*

1538. **Intermittent Treatment of *Trichophyton rubrum* Infections with Griseofulvin**
M. A. COWAN. *British Journal of Dermatology* [*Brit. J. Derm.*] **72**, 185–187, May, 1960. 5 refs.

At the Royal Infirmary, Sheffield, 15 patients with extensive and intractable infection due to *Trichophyton rubrum* were treated with griseofulvin, 7 patients receiving 2 g. daily and 8 receiving 2 g. daily for 2 consecutive days in each week. The condition improved in all cases. Although the total number was insufficient for statistical analysis, it was considered that there was no difference in rate of improvement between the two groups. In one patient in each group there was slight leucopenia and lymphopenia during treatment; also in one patient in

each group atypical lymphocytes were seen occasionally in the peripheral blood on occasions.

The author concludes that the therapeutic results achieved with intermittent administration of griseofulvin are equal to those obtained with continuous therapy, with the added advantage that a smaller quantity of the drug is used at less cost and with less danger of long-term toxic effects. *Benjamin Schwartz*

1539. **Chronic Ringworm Infection of the Skin and Nails Treated with Griseofulvin: Report of a Therapeutic Trial**
B. RUSSELL, W. FRAIN-BELL, C. J. STEVENSON, R. W. RIDDELL, N. DJAVAHISZWILI, and S. L. MORRISON. *Lancet* [*Lancet*] **1**, 1141–1147, May 2, 1960. 1 fig., 16 refs.

A controlled trial [which is notable for its thoroughness] of griseofulvin in the treatment of chronic ringworm infection was carried out in 76 patients (41 male and 35 female) at St. John's Hospital for Diseases of the Skin, London. The drug was given by mouth in a dosage of 1·5 g. daily. In 72 of the patients infection was due to *Trichophyton rubrum*. There was considerable variation in the clinical response, but generally skin lesions were improved by the 8th week, the skin appearing normal by the 16th week, although a few cases remained positive mycologically. Toe-web lesions, however, behaved differently, treatment with griseofulvin for 8 to 48 weeks failing to eradicate infection from 52% of patients harbouring fungus in these sites. Toe-nails failed to become normal in appearance in 26 of 32 treated patients, 11 of whom had been receiving griseofulvin for 44 weeks or longer. Finger-nails responded far better, appearances being normal in 17 out of 22 patients after treatment for 12 to 40 weeks. A diminution in the immediate positive reaction to the trichophytin skin test was observed during treatment in a limited number of patients. No side-effects attributable to griseofulvin were encountered. *E. W. Prosser Thomas*

1540. **Studies in the Epidemiology of Tinea Pedis. III. Cross-infection in the Family**
M. P. ENGLISH and M. D. GIBSON. *British Medical Journal* [*Brit. med. J.*] **1**, 1860–1862, June 18, 1960. 11 refs.

The epidemiology of tinea pedis due to *Trichophyton mentagrophytes* was studied in the families of 22 schoolchildren and in 19 patients attending a skin clinic, all of whom were known to have suffered from the infection. The disease had spread in 3 of the families of the schoolchildren and in 8 of those of the clinic patients. It is considered that two factors were largely responsible for this difference: (1) the families of the clinic patients were in a higher social group than those of the school-children and took more baths per week, which increased the risk of cross-infection; (2) the skin lesions in the school-children were much milder and more easily cured than those of the clinic patients and this too might account for the lower rate of cross-infection in the families of the former. It is suggested that the common mild variety of tinea pedis is not a highly infectious condition. *G. W. Csonka*

1541. **The Treatment of Cutaneous Tuberculosis with Diethyl Dithiol*iso*phthalate: a Preliminary Report**
J. G. COBURN and C. W. MARSDEN. *British Journal of Dermatology* [*Brit. J. Derm.*] **72**, 192–194, May, 1960. 4 figs., 6 refs.

It has been reported that diethyl dithiol*iso*phthalate (ETIP) has an antituberculous effect in mice "comparable to that of isonicotinic acid hydrazide and streptomycin", and when used as an ointment it has a marked effect in some cases of leprosy. The present authors therefore tried an ointment containing ETIP in 5 cases of tuberculosis of the skin seen at Manchester and Salford Hospital for Skin Diseases. The preparation (68% ETIP in magnesium stearate) was applied to the affected area for 10 minutes daily. In 2 patients with lupus vulgaris who had had little previous treatment there was considerable improvement after 5 to 8 weeks; in 2 others who had had extensive treatment previously but who still had active nodules in scar tissue no significant change was observed. Improvement was noted in a patient with scrofuloderma after 2 months, but treatment had to be discontinued because contact sensitivity developed. It is considered that ETIP may be of value in the treatment of cases of lupus vulgaris with minimum scarring. *Benjamin Schwartz*

1542. **Management of Patients with Eczematous Diseases. Use of Soap Versus No Soap**
R. B. STOUGHTON, L. W. POTTS, W. CLENDENNING, S. FISHER, and M. KRESS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **173**, 1196–1198, July 16, 1960. 1 fig., 7 refs.

A controlled study and statistical analysis of 250 patients with four types of eczematous dermatoses (neurodermatitis, contact dermatitis [dermatitis venenata], infantile eczema, and eczematous hand dermatitis failed to show a significant difference in progress of the disease between groups using, respectively, toilet soap or no soap for bathing or washing. While the subjects were on a standard therapeutic regimen, these eczematous dermatoses studied over a 5-week period improved at different average rates, which varied from about 25% for infantile eczema to about 75% for contact dermatitis. After 5 weeks of therapy the improvement rates were definitely lower than during the first week of therapy, and the greatest improvement rate was within the first week of therapy. There was no significant difference between the course of these diseases in winter and in summer.—[Authors' summary.]

1543. **A Clinical Trial of Isothipendyl Hydrochloride (Nilergex) in Dermatology**
J. O. ALEXANDER and G. HARVEY. *Scottish Medical Journal* [*Scot. med. J.*] **5**, 158–161, April, 1960. 7 refs.

From the Royal Infirmary, Glasgow, the authors describe two small clinical trials with isothipendyl hydrochloride ("nilergex"), an antihistaminic which is claimed to have a low incidence of side-effects. The first trial was carried out on 92 patients, of whom 24 had urticaria, 31 sensitization dermatitis, 17 miscellaneous dermatoses, 16 papular urticaria, and 4 Besnier's prurigo;

in a number of these cases the usual local treatment was also given. A small group of 13 cases of similar disorders were treated with a placebo as a control. The response to treatment was assessed as excellent or good in 65 (71%) of the 92 treated cases.

In the second trial 39 patients with the above named skin conditions were treated with isothipendyl hydrochloride and 37 with an inert placebo (using the double-blind technique), the dosage of isothipendyl being 12 to 72 mg. three times a day for 3 weeks in tablet form for adults and for children 6 to 8 mg. daily in the form of a syrup for 2 weeks. A satisfactory response was obtained in 28 (70%) of the treated cases. In adult urticaria there was little difference between the effects of isothipendyl and of the placebo, but in cases of sensitization dermatitis there was a statistically significant difference in results between the treated group and the control group. Side-effects were noted in 17 (13%) of 131 patients followed up, but were severe in only 5. They took the form of drowsiness, a sense of detachment from the environment, generalized weakness, and in one child patient, vomiting. The most satisfactory adult dosage was considered to be between 24 and 48 mg. daily; the daily dose, however, should not exceed 60 mg.

From this small trial the authors formed the impression that isothipendyl is a valuable addition to the treatment of urticaria, sensitization dermatitis, and itching dermatoses and that it is outstanding in the treatment of papular urticaria. In the doses recommended it is relatively free from side-effects. *R. D. Catterall*

1544. **Treatment of Dermatoses with Intravenously Given Methylprednisolone Sodium Succinate**
L. C. GOLDBERG and J. R. BARKOFF. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **172**, 1514–1517, April 2, 1960. 5 refs.

The results of the intravenous administration of methylprednisolone sodium succinate (sodium 6α-methylprednisolone-21-succinate) to 242 patients with 31 different types of dermatosis are reported from the University of Cincinnati Medical School. The patients' ages ranged from 6 months to 93 years and the usual dosage was between 20 and 40 mg. daily, but some patients received as much as 90 mg. daily for 3 weeks. When given intravenously the drug has a half-life of 188 minutes and the same potency, mg. for mg., as when given orally, but in spite of high dosage in some of these cases none of the side-effects such as adrenal atrophy or psychic depression usually noted after oral steroid therapy appeared. It is thought that when given orally a percentage of the drug is converted to cortisone, but that this probably does not happen after intravenous administration. When the drug was given only once every other day or less frequently maintenance doses of adrenal steroids up to 12 mg. daily were also administered orally. Dramatic improvement was obtained in cases of scleroderma, pemphigus foliaceus, lupus erythematosus, pityriasis rosea, psoriasis, and dermatitis medicamentosa and only 18 of the 242 patients showed no or only slight improvement in their dermatosis.
*G. B. Mitchell-Heggs*

1545. **Treatment of Psoriasis with Subdermal Infiltration of Triamcinolone Diacetate Suspension**
A. G. GERARD. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **81**, 535–538, April, 1960. 5 refs.

The effect of local injection of steroids on the inflammatory process in psoriasis is discussed and the results obtained with injection of triamcinolone on local lesions are reported. Initially 0·75 ml. of a suspension of triamcinolone diacetate containing 25 mg. per ml. was deposited in the upper layer of the loose, subcutaneous subdermal tissue under a psoriatic lesion, with resolution of the lesion in 5 to 7 days. Similar results were obtained but with slower resolution (14 to 21 days) with suspensions of triamcinolone containing 5 mg., 2·5 mg., and 1·25 mg. per ml. In the treatment of large plaques a preliminary injection of procaine was found to reduce local discomfort. A persistent residual erythema, which occurred with the initial suspension, was not visible when the strength was reduced. The local injection had no effect on other areas of psoriasis in the same patient.

The number of cases and lesions treated is not specified, but the good response was uniform, the skin remaining clear in all cases for 6 months. At the end of 11 months' observation lesions had reappeared in 16% of cases, but they responded to further treatment. Similar results were obtained with local infiltration of hydrocortisone, but the lesions recurred rapidly. With a combination of triamcinolone and hyaluronidase the results were not materially different from those with triamcinolone only.
*Benjamin Schwartz*

1546. **Some New Principles and Methods of Treatment of Onychomycoses.** (Некоторые новые принципы и методы лечения больных онихомикозами)
A. M. ARIEVIČ, O. G. VIHREVA, B. M. LEBEDEV, and Z. G. STEPANIŠČEVA. *Вестник дерматологии и венерологии* [*Vestn. Derm. Vener.*] **34**, 30–35, May, 1960. 4 figs., 14 refs.

Reviewing current methods of treatment of onychomycoses the authors point out that most of those in use in the U.S.S.R. require the application of bandages, are very painful, and are therefore difficult to use in out-patient clinics. An account is then given of their experience with keratolytic and fungicidal plasters which need only zinc plasters to keep them in contact with the nail and which ensure that the chemicals do not spread over the neighbouring skin, damage to the skin being thus avoided. The plasters used contained 50% salicylic acid, 30% salicylic acid with 20% benzoic acids, and 10% trichloracetic acid. A keratolytic plaster containing 20% urea was also used.

Once the nail was dissolved, fungicidal plasters were applied to the nail bed. This treatment was employed in the treatment of 14 patients, with a total of 173 affected nails. Growth of 120 healthy nails (77%) took place after an average duration of treatment of between 45 and 50 days. *N. Hopewell*

1547. **Anatomy of the Skin 1958.** [In English]
H. PINKUS. *Dermatologica* [*Dermatologica (Basel)*] **120**, 231–254, April [received July], 1960. Bibliography.

# Paediatrics

1548. **Relationship of Neonatal Apnea to Development at Three Years**
C. B. ERNHART, F. K. GRAHAM, and D. THURSTON. *A.M.A. Archives of Neurology* [*A.M.A. Arch. Neurol.*] **2**, 504–510, May, 1960. 1 fig., 9 refs.

The sequelae of perinatal anoxia was studied in 355 children born in the Maternity Hospital, St. Louis, Missouri, who were examined for the purposes of this investigation when they were 3 years old. Of the 355 children 116 had had perinatal anoxia, 159 were normal at birth (born at full term after an easy delivery with an uneventful prenatal and neonatal course), and 80 who had had such complications as haemolytic disease, skull fracture, or intracranial haemorrhage, or who were premature. The criteria on which anoxia was diagnosed were satisfactory. The examination at 3 years was carried out without knowledge of the classification of the infant at birth and included a battery of psychological tests and a neurological examination.

The only significant psychological differences concerned the "cognitive" or "intellectual" functions. There was a greater impairment in conceptual ability than in vocabulary skill in the anoxic children, and their I.Q. score was slightly lower than that of the normal controls. In addition there were more abnormal neurological findings in the anoxic group than in the controls. The authors discuss the possibility of genetic factors being associated with both the perinatal complications and the inferiority found at the age of 3 years.

[This is a carefully planned, controlled study, contributing useful information to knowledge of the sequelae of perinatal asphyxia.] *R. S. Illingworth*

1549. **Bilirubin Studies in Premature Infants Who Received Menadione Derivatives or Vitamin $K_1$ at Birth.** [In English]
H. DYGGVE. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **49**, 230–242, May, 1960. 4 figs., 42 refs.

Total serum bilirubin, haemoglobin values and reticulocyte counts were determined in 317 premature infants receiving different vitamin-K preparations intramuscularly at birth. One hundred and thirty-five of these prematures received 10 mg. of the tetra-sodium salt of 2-methyl-1:4-naphthohydroquinone diphosphate ("synkavit"). One hundred and nine received 10 mg. of an aqueous suspension of vitamin $K_1$ ("konakion") and 73 one mg. of konakion.

The number of premature infants with serum bilirubin values above 20 mg.% was twice as high in the synkavit group as among those receiving vitamin $K_1$. No significant differences were found concerning haemoglobin values, reticulocyte counts, prothrombin times, or number of haemorrhages.

Since hyperbilirubinaemia was previously observed among premature infants who had received 10 mg. of menadione sodium bisulfite, it seems preferable to use vitamin $K_1$ in premature infants instead of water-soluble substitutes with vitamin-K activity.—[Author's summary.]

## CLINICAL PAEDIATRICS

1550. **Clinical Trial to Assess the Effectiveness of Gamma-globulin in Acute Infections in Young Children**
K. C. FINKEL and J. C. HAWORTH. *Pediatrics* [*Pediatrics*] **25**, 798–806, May, 1960. 20 refs.

A controlled clinical trial of gamma-globulin in the treatment of acute infections in children, excluding those with the contagious diseases such as measles, is reported from the Children's Hospital, Winnipeg. An unselected series of 102 children under 2 years of age suffering from acute infections were divided into three comparable groups and treated as follows: Group 1 received a high dosage of gamma-globulin—namely, 0·2 ml. per lb. (0·4 ml. per kg.) body weight intramuscularly within 12 hours of admission, repeated more than once if signs of severe infection persisted; Group 2 were given a low dosage of 0·1 ml. per lb. (0·2 ml. per kg.) body weight in the same way; Group 3 received no gamma-globulin and acted as controls. Antibiotics and other drugs appropriate to the infection were given to the patients in all 3 groups. The particular treatment any individual patient was receiving was not known until after the trial was complete. The groups were comparable and the clinical assessment was standardized. The serum gamma-globulin level was estimated on admission and during and after the illness. There was no significant difference between the two treated groups and the controls in the clinical course of the illness or the recovery time. The presence of physiological hypogammaglobulinaemia in the early months of life was confirmed and a steady increase in the serum gamma-globulin level with increasing age was demonstrated, this last being especially marked in children with a history of previous infections. *Winston Turner*

1551. **The Influence of Glutamic Acid on the Haematopoietic System in Children Suffering from Down's [*sic*] Disease.** (Влияние глютаминовой кислоты на гемопоэтическую систему у детей, страдающих болезнью Дауна)
T. N. VOLKOVA. *Педиатрия* [*Pediatrija*] **38**, 81–84, May, 1960. 13 refs.

The author has found that glutamic acid in doses not exceeding 0·5 g. per kg. body weight improves the general clinical condition of children with "Down's disease" and rectifies the excessive excretion of amino-acids by the kidneys. Care must be taken, however, not to exceed this dose, since evidence is cited to show that

glutamic acid produces intensification of the degenerative process in the red bone marrow. Treatment with doses below 0·5 g. per kg. is accompanied by a rise in erythropoiesis, as shown by the increase in the number of reticulocytes and the rise in haemoglobin value. Above that dosage glutamic acid causes intensive degeneration, with results bordering on complete inhibition of erythropoiesis.

In children up to 7 years of age the response to glutamic acid (after a transient fall in haemoglobin level) results in satisfactory erythropoiesis without increase in the daily excretion of iron; in patients above the age of 7 there is no initial fall in the haemoglobin level, but the later response is less satisfactory, being accompanied by a sharp rise in iron excretion. The reticulocyte response is also less than in the younger patients. In the 15 children with Down's disease described in this paper the dosage of glutamic acid varied from 0·1 to 0·5 g. per kg. It is suggested that 0·5 g. per kg. appears to be the highest dosage and 3 to 4 months the longest period of continuous administration which can be used with safety. *L. Firman-Edwards*

1552. **Coarctation of the Aorta in Infants: a Review of Twelve Years' Experience**
I. H. Glass, W. T. Mustard, and J. D. Keith. *Pediatrics* [*Pediatrics*] **26**, 109–121, July, 1960. 9 figs., 14 refs.

1553. **The Pathogenesis of Hypochromic Anaemias in Early Childhood.** (К вопросу о патогенезе гипохромных анемий у детей раннего возраста)
I. S. Poznjak. *Педиатрия* [*Pediatrija*] **38**, 64–70, May, 1960. 20 refs.

In an investigation of 87 children aged between 3 months and 3 years suffering from hypochromic and normochromic anaemia, 57 were found to have nutritional deficiencies of a qualitative or a quantitative nature, the other 30 having anaemia of infective origin, due to such conditions as upper respiratory infections, otitis media, pneumonia, or toxic dyspepsia; but even in the former group infection also played a part in aggravating the anaemia. The anaemia was hypochromic in 72 cases and normochromic (that is, the colour index was between 0·85 and 1·0) in 15, while 45 cases were classed as mild (haemoglobin value 45 to 60%), 32 as moderate (Hb. 30 to 45%), and 10 as severe (Hb. under 30%). The haemoglobin level, reticulocyte count, serum iron level, and plasma protein levels including globin and haemin content, were determined in all cases.

The nutritional group, in which the anaemia was hypochromic in 32 and normochromic in 15 cases, could be divided into three sub-groups: (1) those with a low serum iron level (10 to 25 $\mu$g. per ml.), a low globin value (3 to 4 g. per 100 ml.) and normal plasma total protein content but diminished haemin values; (2) those with a slightly lowered serum iron level, normal globin and total protein values, but low haemin values; (3) those with a normal colour index but low globin value and diminished total protein levels, whereas the haemin and serum iron values were normal or even raised. The low globin index in Groups 1 and 3 is held to indicate marked changes in protein metabolism, in Group 3 protein deficiency being an additional likely cause of the fall in haemoglobin level. In the infective group, in all of whom the anaemia was hypochromic, the plasma total protein, globin value, and globin index were normal, but the haemin value was low. In these cases the serum iron level varied from subnormal to a markedly raised level (up to 350 $\mu$g. per ml.), indicating, as Robbins and Whipple suggested, that in these cases there is a defect in the synthesis of haemoglobin and a delay in maturation of the erythrocytes in the bone marrow.

All these factors—iron deficiency, protein deficiency, disturbed metabolism of haemin and haemoglobin, and delayed maturation of erythrocytes—must be taken into consideration in the treatment of anaemia. In that due to iron deficiency, iron ascorbinate and aloes with iron are the most satisfactory preparations, and are well assimilated. For children aged 6 months 0·15 to 0·2 g. of iron ascorbinate is an adequate daily dose, but children aged 3 and over require 1 g. daily; the addition of ascorbic acid notably augments the daily increase in haemoglobin level. In the nutritional type of anaemia it is essential to increase the intake of protein (by the intravenous administration of plasma if necessary), as well as to give an adequate supply of vitamins. Treatment should be continued for at least 2 months, especially in iron-deficiency anaemia. In severe cases blood transfusion should accompany the administration of iron. In the normocytic nutritional type of anaemia (Group 3) a diet high in protein and a course of vitamin $B_{12}$ should precede the administration of iron, as in these cases the primary fault lies in the lack of the necessary proteins. *L. Firman-Edwards*

1554. **Epidemic Bronchiolitis in Infants**
M. E. Disney, B. R. Sandiford, J. Cragg, and J. Wolff. *British Medical Journal* [*Brit. med. J.*] **1**, 1407–1411, May 7, 1960. 1 fig., 15 refs.

In two epidemics of infantile bronchiolitis occurring in Birmingham in the winters of 1955–6 and 1956–7 respectively a total of 325 infants under the age of 2 years were treated at Dudley Road Hospital, Birmingham. The clinical picture was that of an upper respiratory infection leading to acute respiratory distress, emphysema, and signs of bronchiolar obstruction. The authors do not consider that the condition can be differentiated from bronchopneumonia either by x-ray examination or by the response to antibiotics.

In the first epidemic 147 patients were treated and 2·7% died; in the second 178 patients were admitted and 5% died. Dehydration, hyperpyrexia, and anoxia developed in the terminal stages; cardiac failure, however, or enlargement of the liver was not considered to be a common cause of death. The necropsy findings were essentially those of obstruction of the finer bronchi and bronchioles by thick mucus. Bacteriological examination of supralaryngeal cough swabs did not reveal a common organism and a search for a possible viral agent was equally unrewarding although in 8 cases evidence of infection by an adenovirus was obtained. Treatment

consisted in administration of oxygen and maintenance of high humidity. Assessment of the value of antibiotics was attempted, although the different groups were not comparable, but it appeared that they were of little value except when a secondary staphylococcal pneumonia supervened.

[No mention is made of the use of bronchodilator drugs although they are briefly referred to in a table. In the abstracter's experience of this common winter illness bronchodilator aerosols and drainage of the bronchi by posture and even by bronchoscopic suction are of the first importance in treatment.]

*H. G. Farquhar*

1555. **Height and Weight of Children with Cerebral Palsy and Acquired Brain Damage**

H. M. STERLING. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **41**, 131–135, April, 1960. 4 figs., 24 refs.

To determine whether the height and weight of children with brain damage differ from those of normal children, the records of 100 children with " cerebral palsy " were compared with similar records for their 53 siblings. Of the 100 affected children 40 were spastic, 55 were athetoid, and 5 had other conditions, the disability being severe in 50, moderately severe in 30, and mild in 20. Height and weight were charted on the anthropometric charts of the Children's Medical Center, Boston, for ages 6 months to 13 years; for those aged 13 to 18 the NEA-AMA (1949) percentile standards were used. The Wetzel grid was also used for those aged 5 to 18.

It was found that children with congenital or early-acquired brain damage tended to group in the shorter height and lighter weight areas, while the unaffected siblings were scattered throughout the range, with a tendency towards greater height and weight than expected. Of the affected children, 77 ranked below the 30th percentile of the charts for height and 73 for weight, in contrast to only 4 of 35 healthy siblings in similar age groups for height and 5 for weight. There was a distinct correlation between the degree of disability and the degree of short height and light weight. A group of 6 children with brain damage acquired after one year of age and not later than 7 years of age were also examined; 3 had heights of 90th percentile rank or greater and 4 had weights of 75th percentile rank or greater. From these findings the author contends that until further detailed metabolic and nutritional studies are carried out on such children the hypothesis of damage to a presumed growth centre or centres is inadequate as an explanation of these findings. *David Morris*

1556. **Acute Bacterial Meningitis in Children: a Controlled Study of Antimicrobial Therapy, with Particular Reference to Combinations of Antibiotics**

R. J. HAGGERTY and M. ZIAI. *Pediatrics* [*Pediatrics*] **25**, 742–747, May, 1960. 2 figs., 9 refs.

The results of experimental and clinical studies have suggested that a combination of antibiotics may be less effective than a single antibiotic in the treatment of acute infections, particularly bacterial meningitis. At the Children's Hospital Medical Center, Boston, 136 patients suffering from acute bacterial meningitis were treated, 65 with a single antibiotic and 71 with antibiotics in combination. The antibiotics used and the dosage constituted the theoretical optimum therapy for the particular infecting organism, where this was isolated. Patients in whom no organism was identified received chloramphenicol alone or chloramphenicol with penicillin. There was no selection of cases; patients admitted on odd dates in the month received a single antibiotic and those admitted on even dates were given a combination. There was no significant difference in clinical response between the patients receiving a single drug and those receiving a combination. No evidence of antagonism between the antibiotics was observed. The authors consider that combinations of antibiotics can safely be given in the treatment of bacterial meningitis in children.

*Winston Turner*

1557. **The Clinical Course, Pathogenesis and Treatment of Epileptic Hemiplegia in Children.** (К клинике, патогенезу и лечению эпилептической гемиплегии у детей)

V. A. KARLOV. *Педиатрия* [*Pediatrija*] **38**, 24–29, May, 1960. 26 refs.

From his personal observations of 50 cases of post-convulsive hemiplegia in children the author, after classifying the disorder under 12 headings, based on the type of onset, the transitory or permanent nature of the hemiplegia, and the subsequent outcome, that is, whether the hemiplegia is progressive or stationary, proposes the following new classification in three main groups. I. Post-epileptic paralysis. (1) Transitory: (*a*) sudden onset; (*b*) slow onset. (2) Permanent: (*a*) pyramidal; (*b*) sub-cortical; (*c*) afferent (cases in this last sub-group show lesions of the post-central cortical regions, with sensory changes but no evidence of motor paresis). II. Paroxysmal epileptic hemiplegia, in which the paralysis is an epileptic equivalent. (1) Type 1, of short duration (less than an hour) and mild. (2) Type 2 lasts some hours or days, during which pyramidal signs are present. III. Pre-convulsive hemiplegia, in which the paresis appears as an epileptic aura. Cases of Group II are rare, and those of Group III still rarer, only one case of the latter being observed in the 50 patients studied.

Of 26 patients treated by the author 22 responded, and in some the hemiplegia practically disappeared. Physical treatment consisted of gymnastics and massage, with active movements, while drug treatment included administration of " mellictin " (to lower muscular tonus), nicotinic acid, " dibasol ", glutamic acid, and anti-convulsants. Aetiologically 10 of these patients were suffering from intra-uterine deformities resulting in Weber's disease, congenital hydrocephalus, platybasia, and sclerotic hemiatrophy, in 7 there was a definite history of birth trauma and in 4 others a probable such history, in 6 a history of cerebral infectious disease (meningitis, encephalitis or arachnoiditis), 7 had suffered severe cranial trauma in early childhood, and 2 had been found to have Rh incompatibility at birth. A family history of epilepsy was present in 7 cases.

*L. Firman-Edwards*

# Medical Genetics

1558. **Genetic Control of Isoniazid Metabolism in Man**
D. A. P. Evans, K. A. Manley, and V. A. McKusick. *British Medical Journal* [*Brit. med. J.*] **2**, 485–491, Aug. 13, 1960. 2 figs., 28 refs.

Plasma isoniazid concentrations have been determined chemically 6 hours after drug ingestion in 484 subjects. The frequency distribution curve of these concentrations is bimodal. Individuals are divided by the antimode into rapid and slow inactivators of isoniazid. There is no heterogeneity for these characters due to sex or age, and on the numbers studied the distribution of phenotypes appears to be the same in American negroes as in whites. The numbers of subjects studied are too small to determine whether tuberculosis affects one phenotype more than another.

Of the subjects studied 267 constitute 53 white families. The family data support the hypothesis that the slow inactivator character is recessive. A "dosage" effect of the allele controlling the dominant character is demonstrable in that there is a significant difference between the mean plasma isoniazid concentration of recognizable heterozygotes and the mean value of all other rapid inactivators. [From the authors' summary.]

1559. **A Genetical Analysis of Thirty Families with Wilson's Disease (Hepatolenticular Degeneration)**
A. G. Bearn. *Annals of Human Genetics* [*Ann. hum. Genet.*] **24**, 33–43, April, 1960. 4 figs., 18 refs.

A genetical analysis has been carried out on 32 patients with Wilson's disease from 30 families obtained largely from the New York area. Fourteen of the 32 patients (43·75%) were of eastern European origin (Jews) and 8 (25·0%) came from the Mediterranean (non-Jews); both groups came from geographically circumscribed areas. A number of differences were observed between the Jews from eastern Europe and the Mediterranean and other groups. The Jews, on an average, tended to have more consanguinity, a later onset of the disease and, consequently, a relatively increased fertility. Clinically there was no predilection for either group to have a particular type of the disease. The Jewish group of patients had an increased variance in the serum copper and ceruloplasmin levels relative to the Mediterranean group. The patients with a normal level of ceruloplasmin came from the Jewish group.

Not all these differences were significant statistically and collection of more cases will be needed before firm conclusions can be drawn. The possibility that the eastern European Jewish population may possess a modifying gene and the possibility that more than one allele is present at the Wilson's disease locus is discussed.

It should be emphasized that the evidence available is insufficient to state that ceruloplasmin is the primary gene product in Wilson's disease. If further evidence lends support to this view it will be necessary to perform structural studies on ceruloplasmin obtained from patients with Wilson's disease of various geographic origins in order to investigate the possibility of chemical allelism.—[From the author's summary.]

1560. **Chromosomal Abnormalities in Father and Mongol Child**
M. Fraccaro, K. Kaijser, and J. Lindsten. *Lancet* [*Lancet*] **1**, 724–727, April 2, 1960. 3 figs., 13 refs.

In the case of a mongol boy the somatic cells had 46 chromosomes, in contrast to the 47 commonly found in mongolism. The mongol's father, an apparently healthy man, was found to have 47 chromosomes in skin cultures. In the mongol there were only 4 short acrocentric chromosomes, instead of 5; but an extra chromosome was present that was similar to those of pairs Nos. 19 and 20. In the father the 47th chromosome was similar to those of pair No. 19.

The father is probably trisomic for chromosome No. 19. The mongol may be trisomic for chromosome No. 19 *and* monosomic for No. 21, or else the extra chromosome may be the product of a reciprocal translocation between 2 chromosomes No. 21. It is not possible, on the evidence available, to decide which hypothesis is correct.

The findings show that fertile, clinically healthy individuals may have a chromosome anomaly and that mongolism may arise from chromosome situations other than the trisomy of chromosome No. 21.—[Authors' summary.]

1561. **A Mongol Girl with 46 Chromosomes**
P. E. Polani, J. H. Briggs, C. E. Ford, C. M. Clarke, and J. M. Berg. *Lancet* [*Lancet*] **1**, 721–724, April 2, 1960. 4 figs., 25 refs.

A mongol girl, selected because she was born from a young mother, in contrast with reported chromosome findings in mongols, had only 46 chromosomes in her bone-marrow cells and had 4 small acrocentric chromosomes like normal females. There were only 5, instead of 6, of the longer acrocentric chromosomes (pairs 14, 15, or 16) but an extra chromosome was present that was not certainly distinguishable from chromosome 12; and this may have carried the major part of the genetic material of chromosome 22.

A reciprocal translocation between chromosomes ?15 and 22 is suggested as the origin of the anomaly. The possibility that it originated during the development of the patient herself is unlikely but not excluded. It is more likely to have occurred in one of the parents, or even a grandparent, possibly during development. If one parent were affected, he or she would be a gonosomic mosaic, and there would be an increased probability of further mongol births, as well as other familial and genetic implications. Were one of the grandparents affected, the genetic implications would be the same, but one of the parents would be distinct in his or her somatic (and germinal) chromosomal make-up.—[Authors' summary.]

# Public Health and Industrial Medicine

1562. **Investigation of Exhaust Gases from Motor Vehicles.** (Исследование выхлопных газов автотранспорта)

M. V. Alekseeva and V. A. Hrustaleva. *Гигиена и Санитария* [*Gig. i Sanit.*] **25**, 10–14, May, 1960. 5 refs.

The authors have investigated the organic compounds present in the air around the exhaust pipes of motor vehicles and on the pavements of city streets, quantitative estimations being made of the content of formaldehyde, acrolein, ketones, aromatic hydrocarbons, total carbon, and carbon monoxide. Carbohydrates and carbon monoxide were estimated by combustion on a platinum coil to carbon dioxide and subsequent titration, formaldehyde by its reaction with chromotropic acid, acrolein by its colour reaction with tryptophan, aromatic hydrocarbons as benzene by Janowski's method, and ketones as acetone by nephelometry. Samples of 0·5 to 1 litre of air were taken by aspiration at a distance of 0·5 metre from the exhaust pipes of various types of motor vehicles using all grades of petrol and diesel oil.

It was found that the air in the vicinity of the motor vehicles contained appreciable concentrations of toxic compounds, and that vehicles using diesel oil emitted much more formaldehyde than those using petrol. Acrolein and acetone were present in the exhaust fumes from vehicles operating on low grade petrol, while large quantities of aromatic hydrocarbons were present in the exhaust of venicles using benzene fuels. The value of catalytic final combustion of exhaust gases in the prevention of atmospheric pollution from this source was demonstrated. Strict supervision of the concentration of organic compounds and carbon monoxide in the air of city streets by the public health authorities is urged. *Basil Haigh*

1563. **Consumption of Medicines on a Working-class Housing Estate**

M. Jefferys, J. H. F. Brotherston, and A. Cartwright. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **14**, 64–76, April [received July], 1960. 2 figs., 9 refs.

The authors first review recent information on the consumption in Great Britain of medicines prescribed under the National Health Service and medicines bought by the public without a prescription. They then report the results of an inquiry, carried out in a post-war housing estate in Hertfordshire in 1954–5, in which a random sample of the population were asked about the medicines consumed over a 4-week period, the illnesses experienced, and the number of consultations with the family doctor. During the 4-week period about one-quarter of the sample had taken medicine prescribed by a doctor and two-thirds had taken medicine not so prescribed. Consumption was higher in women than in men, the sex difference being greatest at age 25 to 45 years. Self-medication was not found to be an alternative to consulting a doctor; individuals who took two or more self-prescribed medicines consulted a doctor more often than those who took less or none. In the majority of instances prescribed medicine was supplemented with self-prescribed drugs.

Children in small families, particularly the first-born, were given more medicines than those in larger families and later born siblings. Mothers who had been educated beyond the minimum provided in elementary and secondary modern schools and wives of black-coated workers gave their children more prescribed and self-prescribed medicines than others. Anxious mothers suffering from " nerves " gave more medicines than those without these personal characteristics.

Laxatives and aspirin were the commonest non-prescribed drugs; 16% of the adults and 26% of the children took laxatives, the figures for aspirin being 39% and 22% respectively. Aspirin was most frequently taken by women between 30 and 50 years of age for a large variety of symptoms. Laxatives appeared to be consumed by children and the elderly more than by the middle-aged subjects; most of the children were given laxatives as a general prophylactic and not because of constipation. *John Fry*

1564. **An Outbreak of Diphtheria: Epidemiological Aspects**

F. L. Groarke, M. I. Adamson, T. F. Elias-Jones, and L. Whittaker. *British Medical Journal* [*Brit. med. J.*] **1**, 1607–1611, May 28, 1960. 4 refs.

A localized epidemic of diphtheria, originating in an infants' school in Barking, Essex, occurred during September and October, 1958. Of the 26 infected individuals (12 patients and 14 carriers), most of whom were detected during mass swabbing of the throats of the school children and their family contacts, 23 were members of the same class, or had a sibling in that class, or were in close contact with a known case or carrier. Only 3 adult carriers were detected and only one of the patients was under school age. Immunization had been carried out in the approved manner with a booster dose (in 1950 and 1954 respectively) in only 2 cases; 9 of the carriers had been actively immunized at some time and 3 had recently been passively immunized by injection of prophylactic serum. Of the 35 pupils in the class 17 had been actively immunized, and of the 127 pupils in the school only 60 could give evidence of immunization. Clearly the disease was associated with the low immunity status of the community at risk, less than 50% of the children having been immunized. As a result of examination of approximately 3,000 throat swabs only one carrier was discovered who was not in close contact with a known case or carrier.

The protective methods employed in this outbreak [which might well be copied in any similar outbreaks] included swabbing of the throats of pupils and staff of the school and of their families and other close contacts, Schick-testing of all pupils in the affected school class with passive-active immunization of those found to be Schick-positive and subsequent active immunization; isolation of all carriers either in hospital or at home; and the treatment of carriers, chiefly with erythromycin, which was successful in all except one whose tonsils and adenoids had to be enucleated before the carrier condition was controlled. Some difficulty was experienced in distinguishing between very mild cases and carriers, particularly in subjects who had recently received chemotherapy.

[This outbreak is of a type which may be expected to occur from time to time in Britain unless a higher proportion of the population are immunized and that immunity maintained.] *H. Stanley Banks*

1565. **The Poliomyelitis Outbreak in Copenhagen in 1952. Epidemiological Studies.** [Monograph, in English]

A. LINDAHL. *Acta medica Scandinavica* [*Acta med. scand.*] **167**, Suppl. 355, 1–167, 1960. 3 figs., bibliography.

1566. **Serologic Status of Children Four Years after Poliomyelitis Field Trial**

G. C. BROWN and J. A. NAPIER. *Journal of Immunology* [*J. Immunol.*] **84**, 463–468, May, 1960. 1 fig., 4 refs.

In this serological study reported from the University of Michigan, Ann Arbor, samples of blood were collected in 1958 from 507 children in the States of Michigan and New York who had participated in the field trial of Salk anti-poliomyelitis vaccine 4 years previously. An inquiry concerning subsequent injections of vaccine and exposure to cases of poliomyelitis resulted in 3 of the children being omitted from the survey because they had been thus exposed.

The sera were then examined for neutralizing antibodies by the metabolic inhibition test using 1:4 as the lowest serum dilution. The children, none of whom had shown detectable antibodies before the field trial in 1954, were divided into 45 groups according to the number of injections of vaccine received in each year and the results of the antibody estimations studied in relation to this grouping.

A high proportion of children in all groups showed antibodies to poliovirus Type 2. Antibodies to poliovirus Type 1 were the next most frequently encountered, although a significant number of children lacked them, especially those not vaccinated within the preceding 2 years. Approximately one-third of all the children showed no antibodies to poliovirus Type 3, although in 1954 they had received a supposedly adequate course of injections, while 9 children were without detectable antibody to any of the three types of poliovirus. Serological studies on 11 children who had through some error received only "placebo" injections in 1954 indicated that, but for intercurrent subclinical infection, the proportion of children lacking antibody to one or more virus types might well have been greater. The authors conclude that most individuals with no history of vaccination in the past 2 or 3 years could well profit by an additional injection of vaccine. *J. E. M. Whitehead*

## INDUSTRIAL MEDICINE

1567. **Changes in the Nervous System in Persons Working with Radioactive Substances.** (О состоянии нервной системы лиц, работающих с радиоактивными веществами)

A. A. DANILIN, N. I. LUKAŠ, T. JA. MALINOVSKAJA, K. B. SKVIRSKAJA, V. D. SEREBRJANNIKOV, and G. A. ŠEŠINA. *Медицинская Радиология* [*Med. Radiol. (Mosk.)*] **5**, 37–43, May, 1960. 1 fig., 13 refs.

Over a period of 5 years examination of the nervous system was periodically carried out in 437 persons working with radioactive substances (total irradiation dose $<0{\cdot}2$ r. per week) and in a control group of 210 individuals not connected in any way with such radioactive substances.

The changes observed in the nervous system during the 5-year period were mainly of a functional character and were practically identical in the two groups, except that the mean incidence of such functional changes was about twice as high among the persons working with radioactive substances. In this latter group also the degree of arterial hypotension was correlated with the duration of exposure to ionizing radiation. Changes in chronaxy indicative of decreased excitability of the peripheral nervous system were observed in 47 of the subjects exposed to ionizing radiation, but in only 17 subjects in the control group. Also a lengthening of optic chronaxy in the exposed group is held to justify the assumption that there was a more profound cortical inhibition in this group than in unexposed subjects.

*A. Orley*

1568. **Oil Folliculitis: a Study of 200 Men Employed in an Engineering Factory**

J. S. FINNIE. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **17**, 130–140, April [received June], 1960. 6 figs., 25 refs.

Little is known about the occupational distribution of oil folliculitis and its severity. The present author has attempted to assess the importance in this condition of occupation, the type and degree of oil exposure, and personal hygiene and to determine whether there is any risk of malignant change in a group of 200 men employed in a machine-tool works in Aberdeen.

Details of home environment, occupational and work history, including previous history of dermatitis, and the various oils used were recorded. The clinical examination was confined to the extensor surface of the forearm, which was washed with soap and water and then examined under Wood's lamp. The results of the skin examination were recorded on charts showing the distribution and intensity of comedones, papules, or other lesions. Using these charts, which were examined in random fashion without reference to the worker's record, the

author classified the cases according to the severity of the skin lesions.

A statistically significant correlation was found between more severe oil folliculitis and the occupations of capstan- and automatic-lathe operators, the men so occupied being exposed to oil to a significant degree. A high proportion of men engaged in drilling had marked folliculitis, but the numbers were too small for statistical confirmation. Age and duration of exposure were of little importance in the development of folliculitis, since there was no significant difference in respect of these factors between the most severely affected occupational groups and the remainder. The majority of the workers used a variety of oils so that it was impossible accurately to observe the effect of different oils. Nevertheless, the automatic-lathe operators (6 men) all had severe folliculitis after exposure predominantly to a highly-viscous, insoluble cutting oil, which may have been a contributory factor.

Personal cleanliness was assessed upon the criteria of the facilities for washing at home; 51 out of the 78 men in the high-risk occupations had adequate access to baths and hot and cold water; this proportion was taken to indicate that these provisions were not an adequate safeguard. In the men most heavily exposed to oil there was a high incidence of earlier attacks of occupational dermatosis. Barrier creams were shown to be ineffective since they were used most frequently by the men in the high-risk occupations. Soap and water did not remove oil from the skin follicles, as demonstrated by photography under ultraviolet light, but apparently a patent industrial skin cleanser was effective in 15 seconds; unfortunately, only 20 of the 200 men made use of this cleanser, so that the skin was never quite free of oil in about 90% of cases.

None of the men examined showed evidence of precancerous or malignant skin lesions, but, the author suggests, this may be explained by the limited period of exposure, the factory having been in operation for under 10 years. *W. K. S. Moore*

1569. **The Effect of Vibration from Electric Drills on Borers in Shale Mines.** (О влиянии вибрации электросверла на организм бурильщика сланцевых шахт)

A. V. Ševal'e, B. M. Šamardin, N. A. Samardina, and H. Ja. Janes. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **4**, 24–26, May, 1960.

Men employed as borers in shale mines use electric rotary drills which were shown to give rise to vibrations at the handle of a frequency of 18 to 20 c.p.s. and an amplitude of 1 to 9 mm. Investigations of the clinical features, the state of the peripheral blood vessels, and the skin reactions were made in 59 borers, aged from 22 to 56 years, and with a working history of 2 weeks to 11½ years.

A comparatively slowly progressive development of a vibration syndrome was observed in these borers, which mainly took the form of disturbances of cutaneous sensation and of the trophic state of the skin in the upper limbs. The angio-spastic component was not pronounced. Other findings included a lowering of the capillary resistance and of the ability of the smaller peripheral vessels to undergo rapid reactive dilatation, increased permeability of the capillaries to plasma proteins, increased capillary fragility, and increased hydrophilia of the skin of the upper limbs. Tests made with adrenaline and histamine showed an increase in the reactivity of the cutaneous vessels to chemical stimuli; this was not confined to the upper limbs directly involved in the work operations, suggesting that the effects of the vibration from the electric rotary drill extend to the body as a whole. The occasional finding of cerebral disturbances, brachial plexus lesions, and paresis of muscles in some cases indicated that there was a direct injurious effect on the central and peripheral nervous systems.

*Basil Haigh*

1570. **Changes in Physiological Functions of Borers in Mines.** (Изменение некоторых физиологических функций у бурильщиков при горно-рудных работах)

I. A. Kovalevic. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **4**, 26–31, May, 1960. 4 figs., 9 refs.

The borers investigated in this study used compressed air percussion drills for boring holes in mines in which the environmental temperature was low (7 to 9° C.) and the relative humidity high (86 to 100%). Tests were carried out for 2 to 5 days on 16 healthy borers before drilling, every hour during drilling, and after completion of their shift and return to the surface, the following factors being investigated: pulse rate, strength of the handgrip by means of a dynamometer, the threshold of excitation of the biceps brachii muscle from the current–time curve, the electromyogram of the thenar muscles of the hand and of the biceps brachii, tetanic spasm of the biceps brachii, and the functional state of the visual analyser. Different types of boring machine were used in the course of the investigation.

The results showed that all the borers suffered adverse effects from the use of these machines, and that these were most marked in those using high-speed percussion drills. The pulse rate was raised and its return to normal was protracted, the grip was weakened, the level of excitation and the mobility of the motor and visual analysers were lowered, and some of the borers who had been engaged on this type of work for 4 years or more showed blanching of the fingers during exposure to cold, and other signs of vibration disease. Various improvements in the design of the boring machines so as to reduce noise, vibration, and chilling of the operator's hands are suggested. A break of 10 minutes after every 1½ to 2 hours of boring is also advised, in addition to a meal-break of 30 minutes during each shift. *Basil Haigh*

1571. **Plastics: the Toxicology of Synthetic Resins.** [Review Article]

R. H. Wilson and W. E. McCormick. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **21**, 536–548, June, 1960. Bibliography.

# Anaesthetics

1572. **Anaesthesia for Thermocoagulation of the Globus Pallidus**
D. G. HURTER. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 160–163, April [received June], 1960. 7 refs.

The author succinctly sums up the four stages of the operation of thermocoagulation for the relief of rigidity and tremor in Parkinson's disease as follows: (1) stereotaxic radiological location of the globus pallidus; (2) craniectomy for access; (3) coagulation; and (4) closure. The specific problems pertaining to each of these procedures are then briefly reviewed. Absence of tremor and rigidity is desirable for satisfactory radiography and therefore demands general anaesthesia, which can also usefully be continued to cover the unpleasantness of bone-nibbling in Stage 2. The impossibility of access to the head during the operation makes endotracheal intubation essential; also because of the proximity and use of electrical apparatus anaesthetic mixtures must be non-explosive, while anaesthesia must be sufficiently deep to cover the strong stimulus of introducing air into the ventricular system and also of moving the patient from the sitting to the supine position. At the same time recovery must be rapid since in Stage 3 the patient must be fully co-operative and free from retching or coughing so that the effect of the lesion on voluntary movement, rigidity, tremor, and speech may be observed.

The author describes a technique he has used in 54 cases treated at the National Hospital for Nervous Diseases, Queen Square, London. Premedication is restricted to atropine only (0·85 mg.) so as to avoid respiratory depression, to facilitate control of the cough reflex, and to minimize postural hypotension. After a sleep dose of thiopentone (average 280 mg.) intubation is performed under suxamethonium, 100 mg., and anaesthesia maintained with nitrous oxide and oxygen in the ratio of 6:2. Pethidine, 10 to 20 mg., is given intravenously as soon as spontaneous respiration returns; great stress is laid on the effectiveness of this small dose in preventing tachypnoea, which, if once allowed to occur, requires an average dose of 31 mg. to abolish it. After the pethidine has become effective halothane is introduced as required to maintain an adequate depth of anaesthesia. Anaesthetized by this technique all patients, with only one exception, became fully awake and co-operative within 15 minutes of withdrawing anaesthesia at the end of Stage 2, while postural hypotension corrected itself rapidly in all but 2 patients, who responded satisfactorily to 5 mg. of methylamphetamine.

*Michael Kerr*

1573. **Atropine in the Treatment of Laryngeal Spasm**
M. ROSEN. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 190–191, April, 1960. 8 refs.

The vagal efferent fibres arise from two distinct sources. The autonomic and somatic parts are merely contiguous during the cervical course of the nerve. There is no evidence that the laryngeal muscles and their nerve supply are in any way structurally different from the striped muscles and their nerves elsewhere in the body. Atropine blocks impulses at postganglionic cholinergic nerve endings, and not at the myoneural junction of striped muscle of which the laryngeal muscles are an example. It should not be expected to, and in clinical doses in our experience does not, relieve laryngeal spasm.

Experimental evidence in favour of the use of atropine, therefore, must be reconsidered. The high dosage used seems to make any apparent effects on laryngeal spasm more likely to be due to central depressant effects. It must be concluded that atropine in clinical doses is of no value in the treatment of laryngeal spasm.—[Author's summary.]

1574. **A Comparison of Inactin and Thiopentone as Intravenous Anaesthetics**
J. W. DUNDEE and J. E. RIDING. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 206–218, May, 1960. 3 figs., 19 refs.

A clinical study of the use of sodium, 5-ethyl, 5′-(1-methyl propyl) thiobarbiturate ("inactin") in 745 patients is presented. Results are compared with those of thiopentone administered to 1,000 patients. Apart from the finding that inactin is only about three-quarters to four-fifths as potent as thiopentone (w/w), no significant differences in the actions of the equipotent doses of the drugs could be detected. The authors conclude that inactin is as satisfactory as thiopentone for routine use in the induction of anaesthesia.—[Authors' summary.]

1575. **Clinical Experiences with 1,1,1 Trichloroethane: a Preliminary Report of 50 Anesthetic Administrations**
W. H. L. DORNETTE and J. P. JONES. *Anesthesia and Analgesia: Current Researches* [*Anesth. Analg. curr. Res.*] **39**, 249–253, May–June, 1960. 1 fig., 1 ref.

This report from the University of Tennessee describes a trial of the halogenated hydrocarbon 1:1:1 trichloroethane for anaesthesia in 50 patients undergoing a variety of elective operations at John Gaston Hospital, Memphis, Tennessee. Premedication was with morphine, or pethidine, and atropine given intramuscularly one hour before operation. Trichloroethane was administered together with nitrous oxide and oxygen (4:1), generally using a special vaporizer. A semi-open (or less often a semi-closed) circuit was employed with a total flow rate of 7·5 to 10 litres per minute. (Soda lime could not be used because of the danger of chemical breakdown of the anaesthetic agent.)

Trichloroethane is non-inflammable and non-irritant to the respiratory passages, and was found to produce a high degree of analgesia. With a concentration of 1 to 2·6% induction of anaesthesia was extremely rapid. Maintenance of light anaesthesia required 0·6 to 2·25%

and this gave sufficient muscular relaxation for extra-abdominal procedures. When D-tubocurarine was required as a supplement its dose could be greatly reduced. After light anaesthesia the reflexes and consciousness returned rapidly. Trichloroethane did not depress the respiration, but it frequently produced a slight, but in some cases a severe, fall in blood pressure. It also frequently caused changes in cardiac rhythm. The authors formed the impression that the disadvantages of this new agent outweigh its advantages, but admit that the series was perhaps too small to allow of definite condemnation.

*Mark Swerdlow*

1576. **Clinical Investigation of Triflupromazine Hydrochloride (Vesprin) as a Preanesthetic Medication**
J. F. ZEEDICK. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **39**, 283–286, May–June, 1960. 3 refs.

This investigation of the value of triflupromazine hydrochloride (" vesprin ") for pre-anaesthetic medication was carried out at St. Francis General Hospital, Pittsburgh, on 43 surgical patients who were divided into four groups, which then received respectively, by intramuscular injection: (1) sodium pentobarbitone, pethidine, and atropine (the control group); (2) triflupromazine (0·2 mg. per kg. body weight), pethidine, and atropine; (3) triflupromazine (0·3 mg. per kg.), pethidine, and atropine; and (4) triflupromazine and scopolamine. All the patients also received 1·4 mg. of sodium pentobarbitone per kg. body weight on the night before operation. On induction of anaesthesia a note was made of the dose of thiopentone required to obtund the eye and lid reflexes.

It was found that in contrast to the 9 control patients the 34 triflupromazine-treated patients appeared calm and co-operative. The induction dose of thiopentone could be reduced in the latter, and also the amount of thiopentone required was less with the higher dose than with the lower dose of triflupromazine and was least in the patients who received premedication with triflupromazine and scopolamine. No significant changes in the blood pressure were observed.

[It would be interesting to see the findings in a much larger series of patients, and also to know the effects of triflupromazine given by itself.] *Mark Swerdlow*

1577. **Myocardial Excitability of Dogs during Cyclopropane Anesthesia: Effect of Diffusion Respiration**
T. D. GRAFF, L. C. HARRIS, N. R. ARBEGAST, and O. C. PHILLIPS. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **39**, 293–301, May–June, 1960. 1 fig., 32 refs.

In an experimental study carried out in the department of anaesthesiology of the Hospital for Women, Baltimore, 10 unpremedicated mongrel dogs were anaesthetized with thiopentone, intubated, and high flows of oxygen administered for 15 minutes to denitrogenate the animals, light anaesthesia being maintained with small doses of 2% thiopentone. A Waters canister was then introduced into the anaesthetic system and cyclopropane administered for 15 minutes, respirations being at first assisted and later controlled. At the end of this period adrenaline was injected intravenously by a standard technique in a dose of 1 μg. per kg. body weight per ml. per 20 seconds until the desired arrhythmia (multifocal ventricular extrasystoles, bigeminal ventricular rhythm, or ventricular tacchycardia) was obtained. The time taken for spontaneous return of normal sinus rhythm was noted. Controlled respiration was then discontinued and the animal allowed to remain apnoeic for 20 minutes; the arrhythmic dose of adrenaline was determined after 5 minutes and again after 20 minutes. The animals were then artificially ventilated for 30 minutes and the provocative dose of adrenaline again noted.

The control pre-apnoeic arrhythmic dose of adrenaline averaged 1·5 μg. per kg. body weight. After 5 minutes of apnoea the average provocative dose was 2·2 μg. per kg., and after 20 minutes' apnoea it was 16·5 μg. per kg. After the 30 minutes' artificial ventilation the average arrhythmic dose of adrenaline was 1·9 μg. per kg. The results are discussed at some length in the light of the findings of other workers. *Mark Swerdlow*

1578. **A Quantitative Study of D-Tubocurarine in Man during Diethyl Ether Analgesia**
F. M. TIERS and J. F. ARTUSIO JR. *Anesthesiology* [*Anesthesiology*] **21**, 256–259, May–June, 1960. 3 figs., 5 refs.

Since the authors first described their technique of administering diethyl ether analgesia for major operations (*J. Amer. med. Ass.*, 1955, **157**, 33; *Abstr. Wld Med.*, 1955, **18**, 169) they have frequently used this analgesia in association with muscle relaxants in patients subjected to abdominal surgery. In this paper from the New York Hospital and Cornell University Medical College, New York, they report a study of the respiratory minute volume in 19 patients given this combination. Recovery from an initial dose of D-tubocurarine averaged 25 minutes regardless of the degree of depression produced, compared with 40 minutes under Plane-1 ether anaesthesia. Recovery from a second equal dose averaged 50 minutes. Summation of effect was seen in all cases, but the duration of effect was decreased by almost 50% from that seen during anaesthesia.

Ether therefore potentiates the action of D-tubocurarine even at the analgesic level, although the duration of the effect is significantly reduced. *W. Stanley Sykes*

1579. **A Clinical Comparison of Chloroform and Halothane by a Blind Study Technique**
B. J. BAMFORTH, K. L. SIEBECKER, J. E. STEINHAUS, and O. S. ORTH. *Anesthesiology* [*Anesthesiology*] **21**, 273–280, May–June, 1960. 3 figs., 14 refs.

Halothane, like chloroform, is a non-explosive and very powerful anaesthetic agent. This investigation, which was carried out at the Medical School, University of Wisconsin, Madison, was designed to determine whether in the routine administration of these two agents it is possible to distinguish them by their clinical effect. Both agents were given as a supplement to gas and oxygen anaesthesia after induction with a thiobarbiturate to 100 patients undergoing neurosurgery, a double-blind

technique being used. Succinylcholine was given for intubation in all cases.

There was a slightly higher incidence of hypotension in the patients given halothane compared with those given chloroform, but bradycardia was more frequent in the latter. There were 6 deaths, 4 after chloroform and 2 after halothane. Of the 4 deaths following chloroform 2 occurred in the operating room, one of them after a massive haemorrhage. The authors were unable to determine the part played by the anaesthetic in these 2 deaths; they state that "it is difficult to exonerate the anaesthetic" . . . but "technical problems of ventilation and blood replacement occupied too great a portion of the attention of the anaesthesiologist".

They did not find it possible to identify the agent solely by its clinical effect, but believe that halothane "bears a strong clinical resemblance to chloroform".

*W. Stanley Sykes*

1580. **Cardiac Arrest following Administration of a High Concentration of Halothane Vapour**

V. T. BAXTER. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 171–180, April [received June], 1960. 5 figs., 27 refs.

The author presents a fully detailed account of a case of cardiac arrest due to a sudden high concentration of halothane in a man aged 59 undergoing left inguinal herniorraphy at the Royal Infirmary, Bristol. The original intention was to maintain anaesthesia with nitrous oxide and oxygen, with hyperventilation and supplementary doses of pethidine and a relaxant drug as required. However, owing to "a lapse in good management" it was necessary to add halothane in moderate concentrations. Four minutes later cardiac arrest occurred but this was effectively corrected by defibrillation, with eventual full recovery. The occurrence of a similar event in another patient 12 hours previously prompted a full-scale investigation of the anaesthetic apparatus. This revealed that there was a fault in the vaporizer which resulted in the delivery of a much higher concentration of halothane than that intended; a detailed and illustrated technical account is given of the mechanical fault concerned, which was due to the loosening of one small although very important screw.

In a review of the consequences of overdosage with halothane the author refers to the different conclusions drawn by various authorities on the association of arrhythmias with the administration of adrenaline in the dog and man under halothane anaesthesia, but concludes that in the present case it seemed unlikely "that adrenaline-induced sensitivity of the patient's myocardium to halothane was responsible for the cardiac arrest". He strongly supports the recommendation of Johnstone and co-workers (Brennan *et al.*, *Lancet*, 1957, **2**, 453; *Abstr. Wld Med.*, 1958, **23**, 67) of giving an intravenous injection of 0·6 mg. of atropine immediately preceding induction with halothane as the minimum safeguard against vagal effects; in fact, the author now keeps a syringe with such a dose ready to hand for use in any case in which halothane may be used. The effect of overdosage of halothane, even cardiac arrest, can readily be offset by washing out the halothane by efficient hyperventilation of the lungs with oxygen.

*Michael Kerr*

1581. **A Clinical Appraisal of 2-Chloroprocaine in Continuous Caudal Obstetrical Anesthesia**

C. W. NELLERMOE, D. C. MOORE, L. D. BRIDENBAUGH, G. N. CASADY, and B. BRALY. *Anesthesiology* [*Anesthesiology*] **21**, 269–272, May–June, 1960. 2 figs., 6 refs.

During 1958 continuous caudal-block analgesia with a 2% solution of 2-chloroprocaine was attempted in 1,030 obstetric patients at the Virginia Mason Hospital, Seattle, Washington. The technique adopted was that described by Moore, in which a malleable needle is used. The initial dose varied from 20 to 50 ml. The onset of anaesthesia was usually within 10 minutes, and the duration was 45 to 90 minutes, the end-point being very sudden. Pain was not relieved in 32 (3·1%) of the patients. Complications occurred in 132 cases (12·8%), including convulsions in 8, in 6 of which they were due to injection of the drug into a vein, and there was one cerebral vascular accident. Referring to the latter the authors emphasize that if vasoconstrictor drugs are given, oxytocic drugs must be omitted, otherwise severe persistent hypertension and even rupture of a cerebral blood vessel may occur in the immediate post-partum period. There were no fatalities in the series.

*W. Stanley Sykes*

1582. **Sore Throat after Anaesthesia**

C. M. CONWAY, J. S. MILLER, and F. L. H. SUGDEN. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 219–223, May, 1960. 2 refs.

A sore throat is one of the more common sequelae of anaesthesia. At Charing Cross Hospital, London, the incidence of sore throat following anaesthesia was studied in 1,259 patients (475 male and 784 female) anaesthetized between September, 1958, and February, 1959. A "mild" sore throat was arbitrarily defined as one lasting for one or two days only and a "severe" sore throat as one which lasted for 3 days or more or was accompanied by loss of voice, hoarseness, or stridor. During the first 3 postoperative days 308 (24·5%) of the patients had a sore throat. There was no significant difference in incidence between the sexes, but sore throat was nearly four times as common in patients who had been intubated (38·2% of 642) as in those who had not (10·2% of 617). The available data did not indicate a possible cause of the sore throat in the non-intubated group, but in the intubated group it was found, unexpectedly, that the incidence of sore throat was high when non-cuffed tubes were used, suggesting that the soreness was due to the greater freedom of movement of these tubes in the trachea. The incidence of sore throat in this group did not appear to be affected by the composition of the tube, the duration of intubation, or the type of laryngoscope used. Insertion of a gauze pharyngeal pack moistened with water and the use of a Ryle's tube were associated with a high incidence of sore throat, whereas anatomical factors expected to make intubation difficult, such as a bull neck, stiff neck, and muscle spasm, were not.

*Michael Kerr*

# Radiology

## RADIODIAGNOSIS

1583. **Some Radiological Aspects of Ischaemia of the Brain**

A. C. BEGG. *British Journal of Radiology* [*Brit. J. Radiol.*] 33, 311–315, May, 1960. 9 figs., 9 refs.

Some aspects of obstructive lesions of the arteries supplying the brain are discussed in this paper from Otago Medical School, Dunedin. When such lesions are situated proximal to the circle of Willis—for instance, in the vertebral or common carotid arteries—the clinical picture is often far from clear cut and the symptoms and signs are frequently mild and vague. The diagnosis of such lesions is no longer of academic interest only, since various forms of medical and surgical treatment are now available. Methods of demonstrating the vertebral arteries are discussed. Direct puncture is not favoured because it is considered somewhat hazardous and fails to demonstrate the proximal part of the course. In the author's experience the best results are obtained on the right side by catheterization of the brachial artery by Seldinger's method, placing the tip of the catheter in the subclavian artery or, if a simultaneous carotid arteriogram is desired, in the innominate artery. On the left side the catheter may be placed in the subclavian artery by either the brachial or the femoral route. Rapid manual injection of 10 ml. of contrast medium has proved satisfactory. For the demonstration of the right carotid system in cases of suspected vascular insufficiency catheterization of the innominate is again a useful procedure. The left common carotid may be demonstrated by catheterization of the subclavian artery via brachial or femoral routes, or by injection of the ascending aorta; if the aorta is injected a manually operated pressure injector, brachial tourniquets, and 15 ml. of contrast medium are used.

These procedures are said to have many advantages—trauma to the vessels supplying the brain is avoided and there is a lower concentration of contrast medium in the brain. In addition, a more complete examination is possible; both the vertebral and carotid systems may be investigated at a single examination and evaluation of the part played by each component of the cerebral circulation is possible. *Arnold Appleby*

1584. **Tumor Localization with Transverse Tomography: Diagnostic and Therapeutic Applications**

B. ROSWIT and S. M. UNGER. *Radiology* [*Radiology*] 74, 705–720, May, 1960. 6 figs., 21 refs.

A radiograph taken in a third dimension by transverse tomography gives information about the extent of local invasion by a neoplasm and may show abnormal stru - tures not visible by other procedures. The authors of this paper from the Veterans Administration Hospital, Bronx, New York, describe their experience of transverse tomography in the diagnosis and location of tumours and its application to surgery and radiotherapy. With the patient erect in the sitting or standing position, the patient and horizontal cassette, on separate stands, are rotated at the same speed in the same direction through 360 degrees during the exposure; the x-ray tube is stationary and is angled downward at 25 degrees. The chief technical difficulties encountered were the maintenance of a precise beam alignment and the need for complete immobilization of the patient; these were overcome by an optical alignment method and a vertical wooden stanchion to which the patient could be fixed by plastic bands.

In the skull and facial regions a meticulous " dissection " is possible so that the extent of more obscure lesions is demonstrated. The authors cite a case in which a recurrent nasopharyngeal carcinoma associated with severe intracranial pain was shown by transverse tomography to be due to invasion of the pterygoid bone; it was relieved by radiotherapy to this localized site. In the thorax the thoracic inlet, upper mediastinum, hilus, and diaphragm, which are incompletely seen by conventional radiography, are well visualized. In a conglomerate shadow of one side of the chest, the peripheral opacity is seen separately from the hilar enlargement. Unsuspected hilar lymph-node enlargement may be demonstrated. In the abdomen and pelvic cavity the best results are obtained after presacral or intraperitoneal instillation of carbon dioxide. Renal, pancreatic, and other retroperitoneal lesions, such as lymph-node involvement in Hodgkin's disease, are well seen.

*Michael C. Winter*

1585. **Water-soluble Radiopaque Media in Roentgenographic Examination of the Alimentary Tract in Infants and Children**

J. L. JARVIS and J. NADELHAFT. *Pediatrics* [*Pediatrics*] 25, 840–851, May, 1960. 13 figs., 3 refs.

During a period of 2½ years the authors have used water-soluble contrast substances in over 500 examinations of the alimentary tract in infants and children at the Babies Hospital, New York. The contrast materials used, all of which proved equally satisfactory, were powdered sodium diatrizoate (" hypaque ") dissolved in normal saline, sodium acetrizoate (" urokon "), sodium and methylglucamine diatrizoates (" renografin "), and an oral preparation of the same compound (" gastrografin "). A satisfactory concentration for the upper alimentary tract was found to be a 25% aqueous solution (weight/volume) and a 6% solution was satisfactory for the large bowel, although other concentrations were used at times. The patients ranged in age from one day to 13 years.

For examination of the oesophagus the medium was introduced through a nasal tube the tip of which was situated at the upper end of the oesophagus. Owing to

the rapid passage of the medium adequate spot films of the distended oesophagus were somewhat difficult to obtain, although the radiographic quality was good. In examination of the stomach satisfactory results were obtained, but mucosal detail was poor and gastric secretions accumulated more rapidly than when barium preparations were used. In studying the small intestine water soluble media were found to be inferior to barium preparations because of dilution and poor mucosal detail. Lastly, in the colon the results were fairly satisfactory, although again mucosal detail was poor. Some of the further advantages are that these water-soluble media do not inspissate in the bowel in cases of obstruction—as may happen with barium preparations—and also if perforation of the bowel occurs they are more easily removed from the peritoneal cavity and no foreign body reaction occurs. They are easy to prepare, cleaner to use, and keep indefinitely, although their bitter taste may be a disadvantage, especially in children.

The authors conclude that these media are preferable to barium preparations for the vizualization of tracheo-oesophageal fistula, congenital pyloric stenosis, megacolon, and the demonstration of narrow tracks and fistulae communicating with the bowel, into which, because of their low viscosity, they penetrate more easily. *Michael C. Winter*

1586. **Mesenteric Vascular Disease**
C. C. WANG and J. D. REEVES. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **83**, 895–908, May, 1960. 8 figs., 18 refs.

The radiological manifestations of mesenteric vascular disease depend on the rapidity and extent of involvement, the size of the vessels involved, the precise anatomical site of narrowing or occlusion, the extent of the available collateral circulation, the integrity of the bowel mucosa, and the presence or absence of bacterial infection of the bowel. The authors of this paper from Massachusetts General Hospital, Boston, consider that the classic picture of a dilated small and large bowel with a sudden arrest of the air-filled column in the transverse colon near the splenic flexure is rare. Cases of arterial insufficiency producing "mesenteric angina" may show little or no change on plain films or in barium studies, while even extensive infarction may or may not produce gaseous distension of the bowel.

They report that in 18 proved cases of the disorder 13 showed only the presence of a non-specific ileus and in only 3 cases were the so-called typical findings observed. The differentiation of arterial from venous occlusion may be very difficult. In some cases typical appearances of mesenteric occlusion simulated large bowel obstruction but barium-enema examination revealed the true nature of the disease. In acute cases barium meal examination may show a marked dilatation of the small bowel with swollen, widely-spaced mucosal folds, while in some flocculation and segmentation of the barium column representing a deficiency pattern may be seen. When a long segment of the bowel is relatively ischaemic, a malabsorption syndrome may or may not be present and the contrast substance may outline a narrowed segment of the bowel with some degree of fixation. These segments may be smooth or at times show multiple punctate ulcerations simulating regional ileitis or ulcerative colitis; they also often show smooth tapering ends continuous with the normal bowel, which may be dilated. Occasionally an intraluminar pseudo-tumour formation can be seen in cases of localized infarction. Aortography may be helpful, but does not necessarily always demonstrate occlusion or diminution of mesenteric vascular flow. *John H. L. Conway-Hughes*

1587. **Findings on Plain Roentgenograms of the Abdomen Associated with Mesenteric Vascular Occlusion with a Possible New Sign of Mesenteric Venous Thrombosis**
S. W. NELSON and W. EGGLESTON. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **83**, 886–894, May, 1960. 8 figs., 7 refs.

The diagnosis of mesenteric vascular occlusion is notoriously difficult. The authors have retrospectively reviewed the radiographs of 21 out of the 49 patients with mesenteric vascular occlusion seen at the Ohio State University Hospital since 1950, and in these have detected abnormal findings on the plain films in more than half the cases. Many of these appearances were non-diagnostic, but they describe a sign observed in 2 cases of proved mesenteric venous occlusion which they consider should suggest the possibility of this condition. This consisted of curvilinear collections of gas in a single loop or in two adjacent narrow-lumen loops of small bowel. In one patient the configuration and location of these collections of gas did not change from one day to the next and also there was no redistribution of the gas when the position of the patient was changed. This finding is regarded as being due to the fact that the segment was very rigid and thick walled; and the constant distance between the two loops is attributed to markedly oedematous walls rather than to intraluminal or intraperitoneal fluid between the loops. Illustrative radiographs are presented. *John H. L. Conway-Hughes*

1588. **Retrograde Enterography: a New Method for the Roentgenologic Study of the Small Bowel**
E. A. GREENSPON and W. LENTINO. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **83**, 909–918, May, 1960. 7 figs., 5 refs.

Writing from Bellevue Hospital, New York, the authors describe a method for examining the small bowel by filling it transnasally with barium from below upwards. This is carried out by means of a standard Miller–Abbott tube so modified that there is no communication of the larger lumen of the tube after the balloon has been inflated, one lumen of the tube being used to inflate the balloon and seal off the bowel and the other for the introduction of the barium suspension or air, or the washing out of the proximal part of the bowel with saline solution. This allows filling of the bowel to be started or stopped at will and post-evacuation or double contrast films to be obtained.

In 16 patients with no previously demonstrable small bowel lesions who were examined by this method an almost diagrammatic precision was obtained. The only difficulty experienced was in the passage of the tube, which is introduced by the nasal route after anaesthesia with 1% " pontocaine ". The patient is instructed to swallow water continuously as the tube is passed down the oesophagus. When the head of the tube is in the stomach the patient is turned on his left side to facilitate the aspiration of stomach contents. He is then turned on his right side, so that gravity can help the passage through the pylorus, and is instructed to swallow ½ to 1 inch (1·25 to 2·5 cm.) of the tube every 15 minutes until the 75-mm. mark reaches the nostril. Aspiration of clear yellow bile, or the fact that there is resistance on inflation of the balloon with 20 ml. of air, indicates that the tip is in the duodenum. The introduction of 3 to 5 ml. of metallic mercury into the balloon before starting to pass the tube was found to help considerably, while the administration of anti-spasmodic or sedative drugs helps the passage through the pylorus. When the balloon is in the third part of the duodenum it is inflated with 20 ml. of air so that it acts as a bolus and the patient is then allowed to push the tube down at the rate of one to 2 feet (30 to 60 cm.) per hour. When in its correct position the balloon is inflated with 50 or 60 ml. of air to seal off the small bowel. It was found that up to 600 ml. of barium suspension could be tolerated, especially if it was introduced slowly at a temperature of 37° C. and in the form of a 1:4 or 1:8 suspension. It is not suggested that this procedure should be employed as a routine, but used only in carefully selected cases, a number of which are described to illustrate the various indications. *John H. L. Conway-Hughes*

1589. **Effective Evacuation of the Colon by a New Therapeutic Agent (Bisacodyl) Proven in Radiology**
O. RAYMOND, B. NOGRADY, and J. A. VÉZINA. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **82**, 1077–1080, May 21, 1960. 4 figs., 8 refs.

In seeking for an improved method of cleansing the lower bowel before performing a barium-enema examination or intravenous pyelography the authors have carried out at the Hôpital du Sacré-Cœur, Montreal, a test with bisacodyl (bis-(*p*-acetoxyphenyl)-2-pyridylmethane; " dulcolax ") on a series of 625 patients, of whom 125 were subjected to pyelography. The results are compared with those obtained with the earlier technique of purgation with castor oil and a colon wash-out. The dosage of bisacodyl was initially 2 tablets, later increased to 3, followed by a bisacodyl suppository on the evening before radiography; next morning a further suppository was given and x-ray examination carried out between one and 2 hours later. No cleansing enema was used.

By this procedure evacuation of the bowel was excellent in 49% of 500 patients, good to satisfactory in 46·8%, and poor in only 4·2%. In an earlier series of 250 cases in which castor oil and colonic wash-out had been employed the corresponding results were: excellent 27·2%, good to satisfactory 52%, and poor 20·8%. Application of the method to the 125 patients undergoing intravenous pyelography, where the object was elimination of gas from the bowel, yielded excellent results in 56·8%, good to satisfactory in 33·6%, and poor results in 8%, compared with 31·2, 44·8, and 24% with the castor-oil method.

The authors are impressed with the effectiveness of this new preparation, not only because of the improved results obtained with it, but also because of the lessening of work for the hospital personnel and the removal of a source of discomfort and even distress to the patient.
*A. M. Rackow*

1590. **The Roentgen Findings in Severe Pseudomembranous Enterocolitis**
S. B. FEINBERG. *Radiology* [*Radiology*] **74**, 778–783, May, 1960. 4 figs., 24 refs.

The radiological appearances in 25 proven cases of pseudomembranous enterocolitis are described in this paper from Mount Sinai Hospital and the University of Minnesota Hospitals, Minneapolis. The aetiology varied; 16 patients had received extensive antibiotic therapy, and in 15 the condition developed after operation. Stress was present in all cases. The author points out that recognition of the x-ray features of pseudomembranous enterocolitis will help in the differential diagnosis and allow appropriate treatment to be started at an early stage, which might possibly be life-saving. Abnormalities were seen radiologically only in severe cases; in 17 of the 25 cases the plain radiograph of the abdomen suggested incomplete or complete intestinal obstruction. There was an area of segmental distension almost always involving the small bowel, which persisted unchanged for days, or until death. This constancy of the distension, it is emphasized, is of particular importance in diagnosis, since it serves to differentiate enterocolitis from early localized paralytic ileus, which either becomes generalized or resolves. Differentiation from mechanical obstruction by radiological examination alone was difficult; but the author states that in some cases of enterocolitis bowel sounds are absent and in others there are irregular bowel sounds.
*Michael C. Winter*

## RADIOTHERAPY

1591. **The Treatment of Carcinoma of the Middle Ear by the 4 MV Linear Accelerator**
K. S. HOLMES. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **53**, 242–244, April, 1960. 2 refs.

In the period 1932–7 carcinoma of the middle ear was treated at the Christie Hospital, Manchester, by the insertion of a radium tube (2 to 5 mg.), giving a dose 5,500 r. at 1 cm.; the fall in dose beyond this distance however is so rapid that large volumes could not be irradiated. In the period 1937–57 multi-field beam-directed x rays at 250 or 500 kV. were used and a tumour dose of 5,000 to 5,500 r. given in 3 weeks, or its equivalent in 5 weeks. However, in 1950 Boden reported late radiation damage to the brain stem after this treatment in 7 patients in whom the dose to the brain stem had been between 4,500 and 6,050 r. He therefore suggested a

dose of 4,500 r. in 3 weeks as the upper limit of safety. Some patients were later treated by a 10-g. radium unit, but the depth dose with this is low.

The present author points out that the physical characteristics of 4-MeV. x rays are such as to overcome all the disadvantages of these methods. Three beam-directed fields are used, one homolateral along the axis of the petrous temporal bone, balanced by contralateral, submandibular, and temporal fields. The dose is 5,000 to 5,500 rads in 3 weeks. A few cases have been treated through two fields with wedge filters. No 5-year results are yet available for treatment with the 4-MeV. linear accelerator. *I. G. Williams*

1592. **Betatron Therapy for Gynaecological Carcinomata.** (Die Betatrontherapie gynäkologischer Karzinome)

G. SCHUBERT, H.-J. SCHMERMUND, and F. OBERHEUSER. *Strahlentherapie* [*Strahlentherapie*] **112**, 4–16, May, 1960. 13 figs., 22 refs.

The authors record their experiences with the 15-MeV. betatron which has been in use at the University Gynaecological Clinic, Hamburg-Eppendorf, since 1955, during which time 347 patients have been treated, 160 with the electron beam and 187 with ultra-hard x rays up to 15-MeV. Those treated with electrons included 43 with breast cancer and 52 with vulvar carcinoma. The dose averaged 300 r. per day and about 15 treatments were given. The range of action of the 15-MeV. electrons is about 80% at a depth of 5 cm. For preoperative irradiation of breast tumours a 20×20-cm. applicator was employed, rice being used as bolus to compensate for the rounded shape of the breast. In this way an almost ideal dose distribution, impossible with any other form of radiation, was obtained. For postoperative therapy an oscillating beam of 9-MeV. electrons was used. In this way a 20-cm. wide " mantle " of radiation was produced that followed the contour of the thorax and extended from the posterior axillary line to the contralateral edge of the sternum. [No details of results are given.] The patients with vulvar carcinoma included 39 with primary and 13 with recurrent lesions. Of the primary cases, the lymph nodes were involved in 28 (70%). A total dose of 5,000 to 6,000 r. was found to be necessary, but the resultant skin peeling healed quickly, leaving moderate induration and telangiectasis. Of 29 cases treated more than one year ago, 5 early cases received inadequate dosage, but of the other 24 patients 18 have survived free from recurrence, some for 2 to 3 years.

The chief use for the supervoltage x-ray beam from the betatron has been in the treatment of pelvic carcinoma. Experiments with a phantom 30 cm. thick and containing pelvic bones showed that when 16-MeV. x rays were applied by means of opposed anterior and posterior fields, the depth dose in the phantom pelvis nowhere fell below 120% of the surface dose, in marked contrast to 200-kV. x rays, with which the depth dose fell to 30%.

Cases treated have included 127 of primary and recurrent carcinoma of the cervix, 12 of carcinoma of the body of the uterus, and 23 of carcinoma of the ovary. Of the 127 cases of carcinoma of the cervix 2 were in Stage I, 5 in Stage II, 58 in Stage III, 10 in Stage IV, and 52 were recurrent. For these cases supervoltage x rays were used, in combination with intra-uterine and vaginal radium applications. The combined dose in the pelvis was nowhere less than 5,000 r., and reached very high levels in the central area; however, no serious bowel or urinary complications have been observed so far. Of 33 patients with Stage-3 carcinoma of the cervix 26 (79%) have survived without recurrence for at least one year and several for 3 years. This one-year survival rate of 79% is compared with the rate of 66% in patients with Stage-3 carcinoma of the cervix treated with 200-kV. irradiation. *E. Stanley Lee*

1593. **The Treatment of Myelomatosis with Lutecium 177**

J. ANDERSON, F. T. FARMER, J. W. HAGGITH, and M. HILL. *British Journal of Radiology* [*Brit. J. Radiol.*] **33**, 374–378, June, 1960. 6 figs., 4 refs.

The results of administration of radioactive lutecium ($^{177}$Lu) in 3 patients suffering from myelomatosis are reported in this paper from King's College Hospital, London, and the Royal Victoria Infirmary, Newcastle upon Tyne. The authors chose $^{177}$Lu because of its physical properties and because it had been shown that in rats about half of an administered dose was concentrated in the skeleton. No preliminary investigation with test doses of $^{177}$Lu was carried out.

The first patient, a man aged 67, with generalized myelomatosis was given 25 mc. of $^{177}$Lu intravenously. After this hypercalcaemia developed, for which prednisone was given. There was then partial relief of pain but the patient died 3 months after treatment with $^{177}$Lu. The second patient, a female aged 59, received 18 mc. of $^{177}$Lu with no effect and then 26 mc. 4 months later. She developed purpura, epistaxis, generalized bleeding, and pancytopenia 28 days after the second dose and died. The third patient, a man of 61, was given 23·5 mc. Pancytopenia developed 25 days later, for which prednisone and antibiotics were administered with some improvement in the blood count. The patient became well enough to be sent to a convalescent home, but while there he developed pain in the back because of collapse of thoracic and lumbar vertebrae and died from bronchopneumonia.

Post-mortem examination in 2 of the cases showed that 25% of the injected $^{177}$Lu was concentrated in the liver and 50% to 65% in the skeleton. An autoradiograph of a section of the skull in one case showed that there was some increase in radioactivity around the periphery of myeloma lesions, such that one large lesion may have received 550 rads to its outer 0·25 mm. while the remainder received only a low dose. *K. E. Halnan*

1594. **Tissue Oxygen Tension and Radiotherapy: a Review and Bibliography Based on a Conference in Burlington, Vermont, August 1958**

P. HOWARD-FLANDERS and O. C. A. SCOTT. *Radiology* [*Radiology*] **74**, 956–963, June, 1960. 32 refs.

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